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Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Please search for method of ~~contraception~~  
by nonmegestrol and/or an ester  
and estradiol or an ester  
  
~~nonmegestrol is also called gestagen~~  
~~estriadiol~~ - - - ~~estrogen~~  
  
~~gestagen + estrogen combination for~~  
~~contraception~~  
~~Species - Nonmegasterol acetate + estradiol~~

Please see attached sheet

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Type of Search

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IG Suite

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Geninfo

SDC

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=&gt; fil embase

FILE 'EMBASE' ENTERED AT 14:15:38 ON 15 MAR 2002  
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FILE COVERS 1974 TO 14 Mar 2002 (20020314/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=&gt; d all tot

L50 ANSWER 1 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

AN 93130379 EMBASE

DN 1993130379

TI [Progestational contraception: Advantages].  
CONTRACEPTION MACROPROGESTATIVE: AVANTAGES.

AU Jamin C.

CS CEGOOP, CMC Foch, Suresnes, France

SO Contraception Fertilite Sexualite, (1993) 21/2 (123-128).  
ISSN: 1157-8181 CODEN: CFSXAE

CY France

DT Journal; (Short Survey)

FS 010 Obstetrics and Gynecology

030 Pharmacology

037 Drug Literature Index

LA French

SL English; French

AB In spite of the nearly total effectiveness of classic estrogen-progestogen oral **contraception** and its good overall tolerance, in a not inconsiderable number of situations yet, it is not possible to resort to it. These situations are the following: high blood pressure, hyperlipidemia, diabetes, minor mastopathy, premenstrual tension either spontaneous or under estroprogestogen therapy. Macroprogestational **contraception** using either pregnanes (chlormadinone acetate) or norpregnanes, promegestone, **nomegestrol acetate**, can be then the right solution. Clinical and metabolic tolerance is excellent. In the occurrence of hypoestrogeny symptoms, a combination of **nomegestrol acetate-estradiol 17 $\beta$ ..**, transdermally administered, has given top results in a preliminary study.

CT Medical Descriptors:

- \*contraception
- \*oral contraception

adult

diabetes mellitus

female

human

hypertension

lipid metabolism

major clinical study

short survey

transdermal drug administration

Drug Descriptors:

- \*chlormadinone acetate: AD, drug administration
- \*estradiol: CB, drug combination
- \*estradiol: AD, drug administration
- \*ethinylestradiol: AD, drug administration
- \*nomegestrol acetate: CB, drug combination
- \*nomegestrol acetate: AD, drug administration
- \*promegestone: AD, drug administration

RN (chlormadinone acetate) 302-22-7, 39864-38-5; (estradiol)  
50-28-2; (ethinylestradiol) 57-63-6; (nomegestrol  
acetate) 58652-20-3; (promegestone) 34184-77-5

CN Lutanyl; Estraderm

L50 ANSWER 2 OF 2 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.  
 AN 92230699 EMBASE  
 DN 1992230699  
 TI [Female **contraception** by a normal dose progestogen in patients over the 40 years of age. Possible association of **nomegestrol acetate/17.beta.-estradiol** by percutaneous route].  
 LA CONTRACEPTION FEMININE PAR PROGESTATIF NORMODOSE APRES 40  
 ANS. POSSIBILITIE D'ASSOCIATION ACETATE DE NOMEGESTROL -  
 17-BETA-ESTRADIOL PAR VOIE CUTANEE.  
 AU Jamin C.  
 CS 169 Bd. Haussmann, 75008 Paris, France  
 SO Revue Francaise de Gynecologie et d'Obstetrique, (1992) 87/6 (370-376).  
 ISSN: 0035-290X CODEN: RFGOAO  
 CY France  
 DT Journal; General Review  
 FS 010 Obstetrics and Gynecology  
 030 Pharmacology  
 037 Drug Literature Index  
 LA French  
 SL French; English  
 AB Although fertility declines with age, the use of an effective **contraceptive** remains necessary in women over 40. Endocrine disorders, which are common in this age group, may also often require control. Conventional estroprogesterogens, even those of the latest generation, cannot be used in women with a high cardiovascular risk, since age cannot be totally excluded as a possible risk factor. The **contraceptive** use of derivatives of 17-hydroxyprogesterone and 19-norprogesterone offer a promising alternative, despite the absence of any exhaustive investigation particularly in situations in which the blood level of **estradiol** has to be reduced. There are, however, some women who respond to this Type of **contraception** by menstrual cycle irregularities, and sometimes by low blood levels of **estradiol**, regardless of the drug used. A preliminary study is described in which 5 mg of **nomegestrol acetate** was combined with 17-.beta.-**estradiol** by transcutaneous route and which has so-far demonstrated sustained **contraceptive** efficacy as well as excellent clinical and metabolic safety.  
 CT Medical Descriptors:  
     \***contraception**  
     adult  
     female  
     human  
     oral drug administration  
     priority journal  
     review  
     transdermal drug administration  
 Drug Descriptors:  
     \***contraceptive agent**  
     \***estradiol: CB, drug combination**  
     \***estrogen**  
     \***gestagen**  
     \***nomegestrol acetate: CB, drug combination**  
     chlormadinone  
     chlormadinone acetate  
     promegestone  
 RN (**estradiol**) 50-28-2; (**nomegestrol acetate**) 58652-20-3; (**chlormadinone**) 1961-77-9;  
     (**chlormadinone acetate**) 302-22-7, 39864-38-5; (**promegestone**) 34184-77-5  
 CN **Lutanyl**; **Surgestone**; **Luteran**; **Estraderm tts**

=> fil medline  
FILE 'MEDLINE' ENTERED AT 14:33:39 ON 15 MAR 2002

FILE LAST UPDATED: 14 MAR 2002 (20020314/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all tot

L83 ANSWER 1 OF 5 MEDLINE  
AN 1999135052 MEDLINE  
DN 99135052 PubMed ID: 9949893  
TI [Biological and clinical safety of **nomegestrol acetate**  
administered alone then associated in inverse sequence with transdermal 17  
beta **estradiol**, in women at risk of dyslipoproteinemia type  
IIa].  
Tolerance biologique et clinique du **Nomegestrol acetate**  
, administre seul puis associe en sequentiel inverse au 17 beta  
**estradiol** cutane, chez des femmes a risque presentant une  
dyslipoproteinemie de type IIa.  
AU Zartarian M; Chevallier T; Micheletti M C; Leber C; Jamin C  
CS Service d'Endocrinologie, Reproduction, Diabetologie, Hopital de l'Archet  
I, Nice.  
SO ANNALES D ENDOCRINOLOGIE, (1998 Dec) 59 (5) 411-6.  
Journal code: 540; 0116744. ISSN: 0003-4266.  
CY France  
DT Journal; Article; (JOURNAL ARTICLE)  
LA French  
FS Priority Journals  
EM 199903  
ED Entered STN: 19990316  
Last Updated on STN: 19990316  
Entered Medline: 19990302  
AB In this study including 26 patients with dyslipoproteinemia classified  
IIa, we evaluated biochemical and clinical safety of **Nomegestrol**  
**acetate (Lutanyl)** used for its antigenadotrophin  
property. It was administered alone, during 3 cycles at the dose of 5 mg/d  
for 21 days by cycle and then it was associated (at the same sequence and  
dose), without any wash out, for the next 6 cycles, with a 17 beta  
**estradiol** patch (Estraderm TTS 50), 50 micrograms/d from the 11th  
to the 21st day of each cycle. **Nomegestrol acetate**,  
alone, had no significant effect on glycemia, antithrombin III,  
triglycerides, total cholesterol, apoprotein A1, and LpA1 values compared  
to those at baseline but apoprotein B and Lp (a) values tended to decrease  
slightly. Serum progesterone levels were collapsed, and FSH values were  
low. Weight and blood pressure remained constant. Adding 17 beta  
**estradiol** enabled to significantly decrease and normalize the  
apoprotein B values after the first 3 cycles compared to the baseline  
values, then these values remained constant during the next 3 cycles.  
There was no effect on the other parameters (except for a significant  
increase in plasmatic **estradiol** values) on the antigenadotrophin  
property of **Nomegestrol acetate**, nor on weight and  
blood pressure which remained constant. Moreover, we observed an important  
decrease in the rate of amenorrheic cycles compared to those with

CT Nomegestrol acetate alone.  
 Check Tags: Female; Human  
 Administration, Cutaneous  
 Adolescence  
 Adult  
 Blood Pressure  
 \*Contraceptives, Oral, Sequential: AD, administration & dosage  
 \*Estradiol: AD, administration & dosage  
 \*Hypercholesterolemia, Familial: CO, complications  
 Middle Age  
 \*Norpregnadienes: AD, administration & dosage  
 \*Progestational Hormones, Synthetic: AD, administration & dosage  
 RN 50-28-2 (Estradiol); 58652-20-3 (TX 066)  
 CN 0 (Contraceptives, Oral, Sequential); 0  
 (Norpregnadienes); 0 (Progestational Hormones, Synthetic)

L83 ANSWER 2 OF 5 MEDLINE  
 AN 1999039971 MEDLINE  
 DN 99039971 PubMed ID: 9822518  
 TI Coadministration of nomegestrol acetate does not diminish the beneficial effects of estradiol on coronary artery dilator responses in nonhuman primates (*Macaca fascicularis*).  
 AU Williams J K; Cline J M; Honore E K; Delansorne R; Paris J  
 CS Department of Comparative Medicine of Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA.  
 SO AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, (1998 Nov) 179 (5) 1288-94.  
 Journal code: 3NI; 0370476. ISSN: 0002-9378.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199812  
 ED Entered STN: 19990115  
 Last Updated on STN: 19990115  
 Entered Medline: 19981223  
 AB OBJECTIVE: Our purpose was to examine the effect of coadministered nomegestrol acetate on estradiol-induced dilator responses of coronary arteries. STUDY DESIGN: In this prospective randomized trial, ovariectomized monkeys were fed a moderately atherogenic diet for 3 months while being treated with (1) no hormone replacement (control, n = 12), (2) estradiol (1.5 mg/d equivalent) added to the diet (n = 12), or (3) estradiol (1.5 mg/d equivalent) plus nomegestrol acetate (3.75 mg/d equivalent) (n = 12) added to the diet. Effects of treatment were measured with analysis of variance. Post hoc analyses were done by multiple comparison tests with Bonferroni corrections. RESULTS: Constrictor responses of epicardial coronary arteries (measured with quantitative angiography) and decreased coronary blood velocity (measured with Doppler ultrasonography) to acetylcholine (10(-6) mol/L) were less in the estradiol-treated monkeys (with or without cotreatment with nomegestrol acetate) than in the untreated monkeys (P <.05). Typical estrogenic responses were induced by estradiol in the endometrium (ie, increased proliferation [Ki-67 expression] [P <.04] and increased hormone receptor expression). These effects were antagonized by nomegestrol acetate. CONCLUSIONS: Although nomegestrol acetate has typical progestin-like effects on the uterus, it does not diminish the beneficial effects of estrogen on acetylcholine-induced dilator responses of coronary arteries.  
 CT Check Tags: Animal; Female; Support, Non-U.S. Gov't  
 Acetylcholine: PD, pharmacology  
 Blood Flow Velocity: DE, drug effects  
 Coronary Angiography  
 Coronary Circulation: DE, drug effects  
 \*Coronary Vessels: DE, drug effects  
 Coronary Vessels: US, ultrasonography  
 Drug Combinations

\*Estradiol: PD, pharmacology  
 Macaca fascicularis  
 \*Norpregnadienes: PD, pharmacology  
 Ovariectomy  
 Prospective Studies  
 Vasoconstriction: DE, drug effects  
 \*Vasodilation: DE, drug effects  
 Vasodilator Agents: PD, pharmacology  
 RN 50-28-2 (Estradiol); 51-84-3 (Acetylcholine); 58652-20-3  
 (TX 066)  
 CN 0 (Drug Combinations); 0 (Norpregnadienes); 0 (Vasodilator Agents)  
  
 L83 ANSWER 3 OF 5 MEDLINE  
 AN 96148040 MEDLINE  
 DN 96148040 PubMed ID: 8571051  
 TI [Pharmacology of oral contraceptives].  
 Pharmacologie des contraceptifs oraux.  
 AU Sitruk-Ware R  
 CS Service d'endocrinologie Hopital, Saint-Antoine, Paris.  
 SO REVUE DU PRATICIEN, (1995 Dec 1) 45 (19) 2401-6.  
 Journal code: T1D; 0404334. ISSN: 0035-2640.  
 CY France  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA French  
 FS F  
 EM 199603  
 ED Entered STN: 19960315  
 Last Updated on STN: 19960315  
 Entered Medline: 19960307  
 AB Oral contraceptives include two types of steroids; ethinyl-estradiol as the main estrogenic component which dose vary from 20 to 50 micrograms per tablet (mostly 30 to 35 micrograms) and progestins essentially derivatives of 19 nortestosterone. Derivatives of 19 norprogesterone such as nomegestrol acetate or ST 1435 are not used as oral contraceptives but are being evaluated through parenteral administration, e.g. implants or transdermal systems. The assessment of the pharmacological properties of these progestins indicate a high antigonadotropic and a high antiestrogenic properties for levonorgestrel and for the newer gestagens as well. Therefore very low doses are being used in the current oral contraceptives. However, there is a lower margin of security with the low dose contraceptives than with previous standard combinations and especially when concomitant medications are ingested such as enzyme-inducing agents. Selection of contraceptive methods should be discussed when specific co-medications are necessary.  
 CT Check Tags: Female; Human  
     Contraceptives, Oral, Synthetic: CL, classification  
     \*Contraceptives, Oral, Synthetic: PD, pharmacology  
     Steroids: AD, administration & dosage  
     Steroids: ME, metabolism  
     Steroids: PD, pharmacology  
 CN 0 (Contraceptives, Oral, Synthetic); 0 (Steroids)  
  
 L83 ANSWER 4 OF 5 MEDLINE  
 AN 95039166 MEDLINE  
 DN 95039166 PubMed ID: 7524930  
 TI [High-dose progestational contraception: advantages].  
     Contraception macroprogestative: avantages.  
 AU Jamin C  
 SO CONTRACEPTION, FERTILITE, SEXUALITE, (1993 Feb) 21 (2) 123-8.  
 Journal code: BUD; 9314045. ISSN: 1165-1083.  
 CY France  
 DT (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 LA French

FS Priority Journals  
 EM 199412  
 ED Entered STN: 19950110  
 Last Updated on STN: 20000303  
 Entered Medline: 19941209  
 AB In spite of the nearly total effectiveness of classic estrogen-progestogen oral **contraception** and its good overall tolerance, in a not inconsiderable number of situations yet, it is not possible to resort to it. These situations are the following: high blood pressure, hyperlipemia, diabetes, minor mastopathy, premenstrual tension either spontaneous or under estroprogestogen therapy. Macroprogestational **contraception** using either pregnanes (chlormadinone acetate) or nor-pregnanes, promegestone, **nomegestrol acetate**, can be then the right solution. Clinical and metabolic tolerance is excellent. In the occurrence of hypoestrogeny symptoms, a **combination** of **nomegestrol acetate-estradiol 17 beta**, transdermally administered, has given top results in a preliminary study.  
 CT Check Tags: Comparative Study; Female; Human  
 Administration, Cutaneous  
 Adult  
 Chlormadinone Acetate: ME, metabolism  
 Chlormadinone Acetate: PD, pharmacology  
 \*Chlormadinone Acetate: TU, therapeutic use  
 Contraceptives, Oral, Combined: ME, metabolism  
 Contraceptives, Oral, Combined: PD, pharmacology  
 Contraceptives, Oral, Combined: TU, therapeutic use  
 Estradiol: BL, blood  
 Estradiol: ME, metabolism  
 Estradiol: PD, pharmacology  
 Estradiol: TU, therapeutic use  
 Incidence  
 Menstruation Disturbances: CI, chemically induced  
 Menstruation Disturbances: EP, epidemiology  
 Norpregnadienes: ME, metabolism  
 Norpregnadienes: PD, pharmacology  
 \*Norpregnadienes: TU, therapeutic use  
 Progestational Hormones, Synthetic: ME, metabolism  
 Progestational Hormones, Synthetic: PD, pharmacology  
 \*Progestational Hormones, Synthetic: TU, therapeutic use  
 Promegestone: ME, metabolism  
 Promegestone: PD, pharmacology  
 \*Promegestone: TU, therapeutic use  
 RN 302-22-7 (Chlormadinone Acetate); 34184-77-5 (Promegestone); 50-28-2  
 (Estradiol); 58652-20-3 (TX 066)  
 CN 0 (Contraceptives, Oral, Combined); 0  
 (Norpregnadienes); 0 (Progestational Hormones, Synthetic)  
 L83 ANSWER 5 OF 5 MEDLINE  
 AN 92335763 MEDLINE  
 DN 92335763 PubMed ID: 1378646  
 TI [Female **contraception** by a normal dose progestogen after 40 years of age. Possible association of **nomegestrol-17-beta-estradiol acetate** by percutaneous route].  
 La **contraception** feminine par progestatif normodose apres 40 ans. Possibilite d'association acetate de **nomegestrol-17-beta-estradiol** par voie cutanee.  
 AU Jamin C  
 CS Service de Gynecologie-Obstetrique, Centre Medico-Chirurgical Foch, Suresnes.  
 SO REVUE FRANCAISE DE GYNECOLOGIE ET D'OBSTETRIQUE, (1992 Jun) 87 (6) 370-6.  
 Journal code: S0H; 0411346. ISSN: 0035-290X.  
 CY France  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA French  
 FS Priority Journals  
 EM 199208

ED Entered STN: 19920904  
 Last Updated on STN: 20000303  
 Entered Medline: 19920820

AB Although fertility declines with age, the use of an effective contraceptive remains necessary in women over 40. Endocrine disorders, which are common in this age group, may also often require control. Conventional estroprogestogens, even those of the latest generation, cannot be used in women with a high cardiovascular risk, since age cannot be totally excluded as a possible risk factor. The contraceptive use of derivatives of 17-hydroxyprogesterone and 19-norprogesterone offer a promising alternative, despite the absence of any exhaustive investigation particularly in situations in which the blood level of estradiol has to be reduced. There are, however, some women who respond to this type of contraception by menstrual cycle irregularities, and sometimes by low blood levels of estradiol, regardless of the drug used. A preliminary study is described in which 5 mg of nomegestrol acetate was combined with 17-beta-estradiol by transcutaneous route and which has so-far demonstrated sustained contraceptive efficacy as well as excellent clinical and metabolic safety.

CT Check Tags: Comparative Study; Female; Human  
 Administration, Cutaneous  
 Adult  
 Age Factors  
 Chlormadinone Acetate: AE, adverse effects  
 \*Contraceptive Agents, Female  
 \*Estradiol: AD, administration & dosage  
 Estradiol: AE, adverse effects  
 Megestrol: AD, administration & dosage  
 Megestrol: AE, adverse effects  
 \*Megestrol: AA, analogs & derivatives  
 Menstruation Disturbances: CI, chemically induced  
 \*Progestational Hormones, Synthetic: AD, administration & dosage  
 Progestational Hormones, Synthetic: AE, adverse effects  
 Promegestone: AE, adverse effects

RN 302-22-7 (Chlormadinone Acetate); 34184-77-5 (Promegestone); 3562-63-8 (Megestrol); 50-28-2 (Estradiol); 58691-88-6 (nomegestrol)

CN 0 (Contraceptive Agents, Female); 0 (Progestational Hormones, Synthetic)

=> fil wpix  
 FILE 'WPIX' ENTERED AT 14:42:35 ON 15 MAR 2002  
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FILE LAST UPDATED: 13 MAR 2002 <20020313/UP>  
 MOST RECENT DERWENT UPDATE 200217 <200217/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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 SEE [<<<](http://www.derwent.com/dwpi/updates/dwpicov/index.html)

=> d all abeq tech tot

DNC C2002-040086  
 TI Oral contraceptive starter kit for ameliorating the problem of breakthrough bleeding and spotting comprises at least two packs comprising an estrogen and progestin.  
 DC B01 B07  
 IN GRUBB, G S  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 96  
 PI WO 2001093848 A2 20011213 (200217)\* EN 13p A61K031-00  
     RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
     NL OA PT SD SE SL SZ TR TZ UG ZW  
     W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
     DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
     KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
     SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW  
     US 2002010167 A1 20020124 (200217) A61K031-56  
 ADT WO 2001093848 A2 WO 2001-US18142 20010605; US 2002010167 A1 Provisional US  
     2000-210310P 20000608, US 2001-872250 20010601  
 PRAI US 2000-210310P 20000608; US 2001-872250 20010601  
 IC ICM A61K031-00; A61K031-56  
 ICS A61K031-57  
 AB WO 200193848 A UPAB: 20020313  
     NOVELTY - An oral contraceptive starter kit comprises at least two cycle packs of oral contraceptives comprising estrogen (I) and a progestin (II). The kit has a first and a last cycle pack. The first cycle pack comprises (I) and (II) greater than the last cycle pack.  
     USE - For ameliorating the problem of breakthrough bleeding and spotting associated with lowest dose estrogen contraceptives.  
     ADVANTAGE - The kit gradually decreases the dose of estrogen over a number of cycles and thus decreases incidences of breakthrough bleeding and spotting that are often associated the low-dose estrogen contraceptives.  
 Dwg.0/0  
 FS CPI  
 FA AB; DCN  
 MC CPI: B01-A02; B01-C03; B01-C04; B01-C05; B01-C06; B14-P01B  
 TECH UPTX: 20020313  
     TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Kit: The cycle packs are packaged in individual units and multiple cycle packs are packaged together as a single unit. The last cycle pack provides a daily dosage of (I) equivalent to 20 microg/dosage unit. The dosage of (I) and (II) in the first cycle pack is greater than in subsequent cycle packs. Also, the dosage of (I) and (II) in the penultimate cycle pack is greater than that of in the last cycle pack. The last cycle pack comprises lowest dosage of (I) and (II). The kit further comprises written instructions describing the order of use of the cycle packs.  
     Preferred Components: The estrogen is ethinylestradiol. The progestin is trimegestone, nomegestrol, norgestrel, levonorgestrel, cyproterone acetate, 3-ketodesogestrel, desogestrel, gestodene, drospirenone, medroxy progesterone acetate, megestrol acetate, norgestimate, 17B diacetyl norgestimate, osaterone, norethindrone, norethindrone acetate, lynestrenol, norethynodrel or ethynodiol diacetate (preferably levonorgestrel, norethindrone, norethindrone acetate, gestodene or norgestimate).  
 L121 ANSWER 2 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD  
 AN 2001-335679 [35] WPIX  
 CR 2001-308583 [31]  
 DNC C2001-103673  
 TI Hormonal composition for treating menopausal estrogen deficiency, osteoporosis and cardiovascular disease, comprises combination of estrogen and progestagen derived from 19-norprogesterone.  
 DC B01

IN PARIS, J; THOMAS, J  
 PA (PARI-I) PARIS J; (SOTH) THERAMEX LAB SA; (THOM-I) THOMAS J  
 CYC 18  
 PI WO 2001030356 A1 20010503 (200135)\* FR 31p A61K031-57  
     RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE  
 ADT WO 2001030356 A1 WO 1999-FR2588 19991025  
 PRAI WO 1999-FR2588 19991025  
 IC ICM A61K031-57  
     ICS A61P005-30  
 AB WO 2001030356 A UPAB: 20010625  
     NOVELTY - Hormonal compositions (A) comprise an orally administered **estrogen-progestagen** combination, allowing the simultaneous administration of an **estrogen** (I) at 0.3-3 mg and a **progestagen** (II) derived from 19-norprogesterone at 0.3-1.5 mg, (I) and (II) being associated or mixed with excipient(s).  
     DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of (A), by combining (I), (II) and excipient(s).  
     ACTIVITY - Osteopathic; cardiant; vasotropic.  
     In tests in menopausal women using 1.5 mg per day of **estradiol** in combination with various doses of **nomegestrol acetate** for 6 months, there was no significant difference in endometrial thickness between groups treated with 0.625, 1.25, 2.5 or 65 mg per day of **nomegestrol acetate**.  
     MECHANISM OF ACTION - None given.  
     USE - (A) is specifically used for treating **estrogen** deficiency, preventing osteoporosis and preventing cardiovascular diseases in menopausal women, by continuous or intermittent administration (all claimed). More generally (A) can be used for treating all types of **estrogen** deficiency in women.  
     ADVANTAGE - Functional disorders caused by menopausal **hypoestrogenia** are controlled while maintaining atrophy of the endometrium and preventing genital bleeding. The required therapeutic effects are obtained using markedly lower doses of (II) than those in related prior art compositions (see FR2754179), so that safety is improved.  
 Dwg.0/0  
 FS CPI  
 FA AB; DCN  
 MC CPI: B01-A02; B01-A03; B01-C04; B14-D01B; B14-F01; B14-N01  
 TECH UPTX: 20010625  
     TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (I) is 17beta-**estradiol** or its ester (specifically the valerate) or an equine conjugated **estrogen**. (II) is **nomegestrol** or its ester (specifically the acetate).  
 L121 ANSWER 3 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD  
 AN 2001-308584 [32] WPIX  
 CR 2001-308582 [31]  
 DNC C2001-095360  
 TI Female **contraceptive** composition comprises **nomegestrol** (or ester) as progestational component and **estradiol** (or ester) as an **estrogenic** component in specific ratios for optimum menstrual cycle control.  
 DC B01  
 IN PARIS, J; THOMAS, J  
 PA (SOTH) THERAMEX LAB SA  
 CYC 92  
 PI WO 2001030358 A1 20010503 (200132)\* FR 27p A61K031-57  
     RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
         NL OA PT SD SE SL SZ TZ UG ZW  
     W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE  
         ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
         LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK  
         SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 ADT AU 2001010335 A 20010508 (200149) A61K031-57  
 ADT WO 2001030358 A1 WO 2000-FR2952 20001024; AU 2001010335 A AU 2001-10335

20001024

FDT AU 2001010335 A Based on WO 200130358

PRAI WO 1999-FR2587 19991025

IC ICM A61K031-57

ICS A61P005-30

AB WO 200130358 A UPAB: 20010831

NOVELTY - Female **contraceptive** compositions (A) comprises **nomegestrol** (or its ester) as progestational component (I) and **estradiol** (or its ester) as **estrogenic** component (II), associated or mixed with a diluent or vehicle, in a weight ratio of (I) to (II) at 0.5-5 (preferably 1-3).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of (A), by combining (I) and (II) with one or more of diluents, filler, compression adjuvants, lubricants and/or disintegrating agents.

ACTIVITY - Antifertility.

Tests in 18-35 year old women having normal menstrual cycles involving administration of **nomegestrol acetate** (Ia) and **estradiol** (IIa) showed that (IIa) at 1.5 mg daily (i.e. a dose insufficient to block **ovulation** if used alone) potentiated the anti-**ovulate** effect of (Ia), so that an adequate **ovulation** inhibiting effect was obtained at low doses of (Ia) (i.e. 0.625 mg per day).

MECHANISM OF ACTION - None given.

USE - (A) are used as **contraceptives**, specifically using a package containing 21-28 tablets of (A) and 0-7 placebo tablets (claimed).

ADVANTAGE - The (I)/(II) ratio is optimized to ensure good control of the menstrual cycle (claimed). The synthetic progestogen (I) are free of metabolic secondary effects. The antigenadotropic action of (I) is potentiated by (II), which also compensates for the **hypoestrogenia** induced by (II).

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-C02; B14-P01B

L121 ANSWER 4 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-308583 [32] WPIX

CR 2001-335679 [31]

DNC C2001-095359

TI Hormonal composition for treating menopausal **estrogen** deficiency, osteoporosis and cardiovascular disease, comprises combination of **estrogen** and progestogen derived from 19-norprogesterone.

DC B01

IN PARIS, J; THOMAS, J

PA (SOTH) THERAMEX LAB SA

CYC 92

PI WO 2001030357 A1 20010503 (200132)\* FR 29p A61K031-57

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE  
ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR  
LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK  
SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001010326 A 20010508 (200149) A61K031-57

ADT WO 2001030357 A1 WO 2000-FR2939 20001024; AU 2001010326 A AU 2001-10326  
20001024

FDT AU 2001010326 A Based on WO 200130357

PRAI WO 1999-FR2588 19991025

IC ICM A61K031-57

ICS A61P005-30

AB WO 200130357 A UPAB: 20010831

NOVELTY - Hormonal compositions (A) comprise an orally administered **estrogen**-progestogen combination, allowing the simultaneous administration of an **estrogen** (I) at 0.3-3 mg and a progestogen (II) derived from 19-norprogesterone at 0.3-1.5 mg, (I) and (II) being associated or mixed with excipient(s).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of (A), by combining (I), (II) and excipient(s).

ACTIVITY - Osteopathic; cardiant; vasotropic.

In tests in menopausal women using 1.5 mg per day of **estradiol** in combination with various doses of **nomegestrol acetate** for 6 months, there was no significant difference in endometrial thickness between groups treated with 0.625, 1.25, 2.5 or 65 mg per day of **nomegestrol acetate**.

MECHANISM OF ACTION - None given.

USE - (A) is specifically used for treating **estrogen** deficiency, preventing osteoporosis and preventing cardiovascular diseases in menopausal women, by continuous or intermittent administration (all claimed). More generally (A) can be used for treating all types of **estrogen** deficiency in women.

ADVANTAGE - Functional disorders caused by menopausal **hypoestrogenia** are controlled while maintaining atrophy of the endometrium and preventing genital bleeding. The required therapeutic effects are obtained using markedly lower doses of (II) than those in related prior art compositions (see FR2754179), so that safety is improved.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-C02; B14-D01B; B14-D01C; B14-F01; B14-N01  
TECH UPTX: 20010611

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Components: (I) is 17 beta-**estradiol** or its ester (specifically the valerate) or an equine conjugated **estrogen**. (II) is **nomegestrol** or its ester (specifically the acetate).

L121 ANSWER 5 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-308582 [32] WPIX

CR 2001-308584 [31]

DNC C2001-095358

TI A female **contraceptive** composition comprises **nomegestrol** (or ester) as progestational component and **estradiol** (or ester) as **estrogenic** component in specific ratios for optimum menstrual cycle control.

DC B01

IN PARIS, J; THOMAS, J

PA (PARI-I) PARIS J; (SOTH) THERAMEX LAB SA; (THOM-I) THOMAS J

CYC 18

PI WO 2001030355 A1 20010503 (200132)\* FR 27p A61K031-57  
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

ADT WO 2001030355 A1 WO 1999-FR2587 19991025

PRAI WO 1999-FR2587 19991025

IC ICM A61K031-57

ICS A61P005-30

AB WO 2001030355 A UPAB: 20010611

NOVELTY - Female **contraceptive** compositions (A) comprise **nomegestrol** (or its ester) as progestational component (I) and **estradiol** (or its ester) as **estrogenic** component (II), associated or mixed with a diluent or vehicle, in a weight ratio of (I) to (II) at 0.5-5 (preferably 1-3).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the production of (A), by combining (I) and (II) with one or more of diluents, filler, compression adjuvants, lubricants and/or disintegrating agents.

ACTIVITY - Antifertility.

Tests in 18-35 year old women having normal menstrual cycles involving administration of **nomegestrol acetate** (Ia) and **estradiol** (IIa) showed that (IIa) at 1.5 mg daily (i.e. a dose insufficient to block ovulation if used alone) potentiated the anti-ovulate effect of (Ia), so that an adequate ovulation inhibiting effect was obtained at low doses of (Ia) (i.e. 0.625 mg per day).

MECHANISM OF ACTION - None given.

USE - (A) are used as **contraceptives**, specifically using a package containing 21-28 tablets of (A) and 0-7 placebo tablets (claimed).

ADVANTAGE - The (I)/(II) ratio is optimized to ensure good control of the menstrual cycle (claimed). The synthetic progestogen (I) are free of metabolic secondary effects. The antagonadotropic action of (I) is potentiated by (II), which also compensates for the **hypoestrogenia** induced by (II).

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-A02; B01-C02; B14-P01B

L121 ANSWER 6 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-040884 [05] WPIX

DNC C2001-011807

TI Method of **contraception** and for e.g. treating secondary amenorrhea, dysfunctional bleeding and endometriosis comprises administering progestational agent and bicyclic heterocyclic antiprogestin compound.

DC B01 B02

IN EDWARDS, J P; FENSOME, A; GRUBB, G S; JONES, T K; SANTILLI, A A; TEGLEY, C M; VIET, A Q; WROBEL, J E; ZHANG, P; ZHI, L; MARSCHKE, K B

PA (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC

CYC 93

PI WO 2000066225 A1 20001109 (200105)\* EN 70p A61P015-18

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000051251 A 20001117 (200111) A61P015-18

EP 1173253 A1 20020123 (200214) EN A61P015-18

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
RO SE SI

ADT WO 2000066225 A1 WO 2000-US11846 20000501; AU 2000051251 A AU 2000-51251  
20000501; EP 1173253 A1 EP 2000-935851 20000501, WO 2000-US11846 20000501

FDT AU 2000051251 A Based on WO 200066225; EP 1173253 A1 Based on WO 200066225

PRAI US 2000-552545 20000419; US 1999-305007 19990504; US 1999-198246  
19990504

IC ICM A61P015-18

ICS A61K031-565; A61K031-57; A61K045-06

ICI A61K031:565; A61K031:565; A61K031:54; A61K031:535; A61K031-57; A61K031-57

AB WO 200066225 A UPAB: 20010124

NOVELTY - Method of **contraception** comprises administration to a female for 28 consecutive days of:

(1) 14-24 daily doses of a progestational agent equal in activity to 35-100  $\mu$ g levonorgestrel;

(2) 1-11 daily doses of 2-50 mg bicyclic heterocyclic antiprogestin compound (I) and

(3) optionally a placebo for the remainder of 28 days.

DETAILED DESCRIPTION - Method of **contraception** comprises administration to a female for 28 consecutive days of:

(1) 14-24 (preferably 21) daily doses of a progestational agent equal in activity to 35-100  $\mu$ g levonorgestrel;

(2) 1-11 (preferably 3) daily doses of 2-50 mg bicyclic heterocyclic antiprogestin compound of formula (I) and

(3) optionally a placebo for the remainder (preferably 4) of the 28 days.

A, B = S, CH or N, provided that when A = S then B = CH or N, when B = S then A = CH or N and that both are not CH and when both are N then one is optionally substituted by 1-6C alkyl;

R<sub>1</sub>, R<sub>2</sub> = H or 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl, aryl or heterocyclyl (all optionally substituted), CORA or NRBCORA or

R<sub>1</sub> + R<sub>2</sub> = 3-8C spiroalkyl, 3-8C spiroalkenyl or 3-8 membered

spiroheterocyclyl ring containing 1-3 O, S or N) heteroatoms;  
 RA = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all optionally substituted);  
 RB = H or optionally substituted 1-3C alkyl;  
 R3 = H, OH, NH<sub>2</sub>, optionally substituted 1-6C alkyl, optionally substituted 3-6C alkenyl, optionally substituted 3-6C alkynyl or CORC;  
 RC = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all optionally substituted);  
 R4 = phenyl substituted by X, Y and Z or 5- or 6-membered ring containing 1-3 O, S, SO, SO<sub>2</sub> or NR<sub>5</sub> heteroatoms and optionally substituted by 1 or 2 halo, CN, NO<sub>2</sub>, 1-3C alkyl, 1-3C alkoxy, 1-3C aminoalkyl, CORF or NRGCORF;

X = halo, CN, optionally substituted 1-3C alkyl, optionally substituted 1-3C alkoxy, optionally substituted 1-3C thioalkyl, optionally substituted 1-3C aminoalkyl, NO<sub>2</sub>, 1-3C perfluoroalkyl, 5-6 membered heterocyclyl containing 1-3 heteroatoms, CORD, OCORD or NRECORD;

RD = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all optionally substituted);

RE = H or optionally substituted 1-3C alkyl;

Y, Z = H, halo, CN, NO<sub>2</sub>, 1-3C alkoxy, 1-3C alkyl or 1-3C thioalkyl;

RF = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all optionally substituted);

RG = H or optionally substituted 1-3C alkyl;

R5 = H or 1-3C alkyl and

W = O or a bond

INDEPENDENT CLAIMS are included for the following:

(A) a method of **contraception** which comprises administration to a female of 18-21 daily doses of a progestational agent equivalent to 35-100 mu g levonorgestrel and 10-35 mu g ethinyl **estradiol**, 1-7 daily doses of 2-50 mg (I) and optionally a placebo for the remainder of the 28-day cycle;

(B) a method of **contraception** which comprises administration to a female of 18-21 daily doses of a progestational agent equivalent to 35-150 mu g levonorgestrel and 10-35 mu g ethinyl **estradiol**, 1-7 daily doses of 2-50 mg (I) and 10-35 mu g ethinyl **estradiol** and optionally a placebo for the remainder of the 28-day cycle and

(C) kits for the above methods.

ACTIVITY - Gynecological; cytostatic; anabolic.

USE - Useful for contraception and for treating secondary amenorrhea, dysfunctional bleeding, uterine leiomyomata, endometriosis, polycystic ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon or prostate and minimizing the side effects of menstrual bleeding. The methods are also useful for stimulating food intake.

Dwg.0/0

FS CPI  
 FA AB; GI; DCN  
 MC CPI: B01-A02; B01-C03; B01-C05; B01-C06; B01-C09; B06-H; B14-E11; B14-H01;  
 B14-N14; B14-P02

TECH UPTX: 20010124

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred drugs: (I) Comprises 6-(3-chlorophenyl)-1,4-dihydro-4,4-dimethyl-2H-thieno(2,3-d)(1,3)oxazine-2-one (Ia).

The progestational agent is levonorgestrel, norgestrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, norethindrone acetate, norgestimate, osaterone, cyproterone acetate, trimegestone, dienogest, drospirenone, **nomegestrol** or 17-deacetylnorgestimate.

L121 ANSWER 7 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-031720 [04] WPIX

DNC C2001-009622

TI Method of **contraception** and for treating e.g. secondary amenorrhea, dysfunctional bleeding and endometriosis by administering progestational agent and antiprogestin .

DC B02

IN EDWARDS, J P; FENSCOME, A; GRUBB, G S; JONES, T K; PUWEN, Z; SANTILLI, A A;

PA TEGLEY, C M; TERESENKO, E A; VIET, A Q; WROBEL, J E; ZHI, L  
 (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC  
 CYC 93  
 PI WO 2000066103 A2 20001109 (200104)\* EN 61p A61K031-00  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2000046749 A 20001117 (200111) A61K031-00  
 EP 1173208 A2 20020123 (200214) EN A61K045-06  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI  
 ADT WO 2000066103 A2 WO 2000-US11449 20000501; AU 2000046749 A AU 2000-46749  
 20000501; EP 1173208 A2 EP 2000-928519 20000501, WO 2000-US11449 20000501  
 FDT AU 2000046749 A Based on WO 200066103; EP 1173208 A2 Based on WO 200066103  
 PRAI US 2000-552037 20000419; US 1999-198238 19990504  
 IC ICM A61K031-00; A61K045-06  
 ICS A61K031-12; A61K031-495; A61K031-565; A61K031-57; A61P015-18  
 ICI A61K031-57, A61K031:495, A61K031:565; A61K031-57, A61K031:12, A61K031:565  
 AB WO 200066103 A UPAB: 20010118  
 NOVELTY - **Contraception** comprises administration to a female for  
 28 consecutive days:  
 (1) 14-21 daily doses of a progestational agent equivalent to 35-100  
 mu g levonorgestrel;  
 (2) 1 to 11 daily doses of 2-50 mg of an antiprogestin bicyclic  
 heterocyclic compound (I) or its salts and  
 (3) optionally a placebo for the remainder of the 28-day cycle.  
 DETAILED DESCRIPTION - **Contraception** comprises  
 administration to a female for 28 consecutive days:  
 (1) 14-21 daily doses of a progestational agent equivalent to 35-100  
 mu g levonorgestrel;  
 (2) 1 to 11 daily doses of 2-50 mg of an antiprogestin bicyclic  
 heterocyclic compound of formula (I) or its salts and  
 (3) optionally a placebo for the remainder of the 28-day cycle.  
 A, B, D = N or CH, provided that not all are CH;  
 R1, R2 = H or 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C  
 cycloalkyl, aryl or heterocyclyl (all optionally substituted), CORA or  
 NRBCORA or  
 R1 + R2 = 3-8C spiroalkyl, 3-8C spiroalkenyl or 3- to 8-membered  
 spiroheterocyclyl ring containing 1-3 O, S or N heteroatoms (all  
 optionally substituted by 1-4 F, 1-6C alkyl, 1-6C alkoxy, 1-6C thioalkyl,  
 CF3, OH, CN, NH2, 1-6C alkylamino or di-(1-6C alkyl)-amino);  
 RA = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all  
 optionally substituted);  
 RB = H or optionally substituted 1-3C alkyl;  
 R3 = H, OH, NH2, optionally substituted 1-6C alkyl, optionally  
 substituted 3-6C alkenyl or CORC;  
 RC = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all  
 optionally substituted);  
 R4 = phenyl substituted by X, Y and Z or 5- or 6-membered ring  
 containing 1-3 O, S, SO, SO2 or NR5 heteroatoms and optionally substituted  
 by 1-2 halo, CN, NO2, 1-3C alkyl, 1-3C alkoxy, 1-3C aminoalkyl, CORF or  
 NRGCORF;  
 X = halo, CN, optionally substituted 1-3C alkyl, optionally  
 substituted 1-3C alkoxy, optionally substituted 1-3C thioalkoxy, NH2,  
 optionally substituted 1-3C aminoalkyl, NO2, 1-3C perfluoroalkyl, 5- to  
 6-membered heterocyclyl (containing up to 3 heteroatoms), CORD, OCORD or  
 NRECORD;  
 RD = H or 1-3C alkyl, aryl, alkoxy or 1-3C aminoalkyl (all optionally  
 substituted);  
 RE = H or optionally substituted 1-3C alkyl;  
 Y, Z = H, halo, CN, NO2, 1-3C alkoxy, 1-3C alkyl or 1-3C thioalkoxy;  
 RF = H or 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all  
 optionally substituted);

RG = H or optionally substituted 1-3C alkyl;  
 R5 = H or 1-3C alkyl;  
 Q = O, S, NR6 or CR7R8 and  
 W = O or a bond.

INDEPENDENT CLAIMS are included for the following:

(1) a method of **contraception** which comprises administering a first phase of 18-21 (preferably 21) daily dosage units of a progestational agent equivalent to 35-150  $\mu$ g levonorgestrel and ethinyl **estradiol** at a daily dosage of 10-35  $\mu$ g, a second phase of 1-7 (preferably 3) daily dosage units of (I) at a daily dosage of 2-50 mg and optionally a placebo for the remainder (preferably 4 daily dosage units) of a 28 day period;

(2) a method of **contraception** which comprises administering a first phase of 18-21 (preferably 21) daily dosage units of a progestational agent equivalent to 35-150  $\mu$ g levonorgestrel and ethinyl **estradiol** at a daily dosage of 10-35  $\mu$ g, a second phase of 1-7 (preferably 3) daily dosage units of (I) at a daily dosage of 2-50 mg and ethinyl **estradiol** at a concentration of 10-35  $\mu$ g and optionally a placebo for the remainder (preferably 4 daily dosage units) of a 28 day period and

(3) kits for daily oral administration as above.

ACTIVITY - Gynecological; cytostatic; anabolic.

USE - Useful for contraception and for treating secondary amenorrhea, dysfunctional bleeding, uterine leiomyomata, endometriosis, polycystic ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon or prostate and minimizing the side effects of menstrual bleeding. The methods are also useful for stimulating food intake.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-A02; B01-C03; B01-C04; B01-C05; B01-C06; B01-C09; B06-A03;  
 B06-E03; B06-H; B14-E11; B14-F02; B14-H01; B14-N14; **B14-P01**  
 ; **B14-P01B**

TECH UPTX: 20010118

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred drugs: (I) Comprises 6-(3-chlorophenyl)-4,4-dimethyl-1,4-dihydro-3-oxa-1,8-diaza-naphthalene-2-one (Ia).

The progestational agent comprises levonorgestrel, norgestrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, norethindrone acetate, norgestimate, osaterone, cyproterone acetate, trimegestone, dienogest, drospirenone, **nomegestrol** or 17-deacetyl norgestimate.

L121 ANSWER 8 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-024743 [03] WPIX

CR 2001-024742 [63]

DNC C2001-007495

TI **Contraceptive** compositions comprise quinazolinone and benzoxazine derivatives and is also useful for treatment/prevention of conditions such as amenorrhea, dysfunctional bleeding, uterine leiomyomata, carcinomas and endometriosis.

DC B01 B02

IN EDWARDS, J P; FENSOME, A; GRUBB, G S; JONES, T K; TEGLEY, C M; TERESENKO, E A; WROBEL, J E; ZHANG, P; ZHI, L

PA (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC

CYC 93

PI WO 2000066165 A1 20001109 (200103)\* EN 101p A61K045-06

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000045011 A 20001117 (200111) A61K045-06

EP 1173206 A1 20020123 (200214) EN A61K045-06

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI

ADT WO 2000066165 A1 WO 2000-US11644 20000501; AU 2000045011 A AU 2000-45011  
 20000501; EP 1173206 A1 EP 2000-926488 20000501, WO 2000-US11644 20000501  
 FDT AU 2000045011 A Based on WO 200066165; EP 1173206 A1 Based on WO 200066165  
 PRAI US 2000-552357 20000419; US 1999-183042 19990504  
 IC ICM A61K045-06  
 ICS A61K031-57; A61P015-18  
 ICI A61K031:565; A61K031:565; A61K031:565; A61K031:535; A61K031:495;  
 A61K031:47; A61K031-57; A61K031-57; A61K031-57

AB WO 200066165 A UPAB: 20020301

NOVELTY - **Contraceptive** compositions comprise quinazolinone and benzoxazine derivatives and is also useful for treatment/prevention of conditions such as amenorrhea, dysfunctional bleeding, uterine leiomyomata, carcinomas and endometriosis.

DETAILED DESCRIPTION - A method of **contraception** comprises administering to a female of child bearing age for 28 consecutive days:

- (a) a first phase of 14-24 daily dosage units of a progestational agent equal to 35-100 microgram levonorgestrel;
- (b) a second phase of 1-11 daily dosage units, at a daily dosage of 2-50 mg of an antiprogestin compound of formula (I) or its pharmaceutically acceptable salt

R1, R2 H, optionally substituted 1-6C alkyl, optionally substituted 2-6C alkenyl or alkynyl, optionally substituted 3-8C cycloalkyl, aryl, optionally substituted heterocyclic, CORA or NRBCORA; alternatively R1 and R2 are fused to form: (a) optionally substituted 3-8 membered spirocyclic alkyl ring; (b) optionally substituted 3-8 membered spirocyclic alkenyl; or (c) optionally substituted 3-8 membered heterocyclic ring containing 1-3 heteroatoms selected from O, S and N; the rings of (a), (b) and (c) are optionally substituted by 1-4 groups selected from F, 1-6C (alkyl, alkoxy or thioalkyl), CF<sub>3</sub>, OH, CN, NH<sub>2</sub>, -NH(1-6C alkyl) or -N(1-6Calkyl)<sub>2</sub>; RA is H, optionally substituted (1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl); RB is H or optionally substituted 1-3C alkyl; R3 = H, OH, NH<sub>2</sub>, optionally substituted(1-6C alkyl, 3-6C alkenyl or alkynyl) or CORC; RC = H, optionally substituted (1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl); R4 = H, halogen, CN, NO<sub>2</sub>, optionally substituted (1-6C alkyl, alkynyl, 1-6C alkoxy or 1-6C aminoalkyl) or amino; R5 = (a) or (b); (a) is trisubstituted benzene of formula (II) X = halogen, CN, optionally substituted (1-3C alkyl, alkynyl, 1-3C alkoxy, 1-3C thioalkoxy, 1-3C aminoalkyl), NO<sub>2</sub>, 1-3C perfluoroalkyl, 5 or 6 membered heterocyclic ring containing 1-3 heteroatoms, CORD, OCORD or NRECORD; RD = H, optionally substituted (1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl); RE = H or optionally substituted 1-3C alkyl; Y, Z = H, halogen, CN, NO<sub>2</sub>, amino, aminoalkyl, 1-3C alkoxy, 1-3C alkyl or 1-3C thioalkoxy; (b) is 5 or 6 membered ring with 1,2, or 3 heteroatoms selected from O, S, SO<sub>2</sub>, or NR6 and containing 1 or 2 independent substituents selected from H, halogen, CN, NO<sub>2</sub>, amino, 1-3C alkyl, 1-3 C alkoxy, 1-3C aminoalkyl, CORF or NRGCORF; RF = H, optionally substituted(1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl); RG = H or optionally substituted 1-3C alkyl; R6 = H or 1-3C alkyl; G1 = O, NR7 or CR7R8; G2 = CO, CR7R8 provided that when G1 is O, G2 is CR7R8 and G1 and G2 cannot be both CR7R8; R7 and R8 = H or optionally substituted alkyl, aryl or heterocyclic moiety;

(c) optionally a third phase of daily dosage units of an orally and pharmaceutically acceptable placebo for the remaining 28 consecutive days in which no antiprogestin, progestin or **estrogen** is administered. The total daily dosage units of the first, second and third phase equals 28.

INDEPENDENT CLAIMS are is also included for:

(1) a method of **contraception** comprising administering to a female of child bearing age over a period of 28 consecutive days:

- (a) a first phase of 18-21 daily dosage units of progestostational agent equal in progestational activity to 35-150 microgramme levonorgestrel and ethinyl **estradiol** at a daily dosage of 10-35 microgramme; and
- (b) a second phase of 1-7 daily dosage units of an antiprogestin of above claim at a daily dose of 2-50 mg; and
- (c) optionally an orally and pharmaceutically acceptable placebo for each remaining day of the 28 consecutive days;

(2) a method of **contraception** comprising administering to a female of child bearing age over a period of 28 consecutive days:

(a) (a) a first phase of 18-21 daily dosage units of progestostational agent equal in progestational activity to 35-150 microgramme levonorgestrel and ethinyl **estradiol** at a daily dosage of 10-35 microgramme; and

(b) a second phase of 1-7 daily dosage units of an antiprogestin of above claim at a daily dose of 2-50 mg and ethinyl **estradiol** at a concentration of 10-35 microgramme; and

(c) optionally an orally and pharmaceutically acceptable placebo for each remaining day of the 28 consecutive days, total daily dosage units being 28;

(3) a pharmaceutically useful kit adapted form daily oral administration comprising:

(1) a first phase of 14-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 microgramme of levonorgestrel;

(2) a second phase of 1-11 daily dosage units of an antiprogestin compound as above, each daily dosage unit comprising an antiprogestin compound at a daily dosage 2-50 mg; and

(3) a third phase of daily dosage units of an orally and pharmaceutically acceptable placebo. The total number of the daily dosage units in the three phases equals 28;

(4) a pharmaceutically useful kit adapted form daily oral administration comprising:

(a) a first phase of 18-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 microgramme of levonorgestrel and ethinyl **estradiol** at a daily dose of 10-35 microgramme;

(b) a second phase of 1-7 daily dosage units of an antiprogestin compound as above, each daily dosage unit comprising an antiprogestin compound at a daily dosage 2-50 mg; and

(c) a third phase of 0-9 daily dosage units of an orally and pharmaceutically acceptable placebo. The total number of the daily dosage units in the three phases equals 28; and

(5) a pharmaceutically useful kit adapted form daily oral administration comprising:

(a) a first phase of 18-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 microgramme of levonorgestrel and ethinyl **estradiol** at a daily dose of 10-35 microgramme;

(b) a second phase of 1-7 daily dosage units of an antiprogestin compound as above, each daily dosage unit comprising an antiprogestin compound at a daily dosage 2-50 mg and ethinyl **estradiol** at a concentration of 10-35 microgramme; and

(c) a third phase of 0-9 daily dosage units of an orally and pharmaceutically acceptable placebo. The total number of the daily dosage units in the three phases equals 28.

ACTIVITY - Gynecological; cytostatic.

MECHANISM OF ACTION - **contraceptive**; anticancer agent.

USE - The methods are useful for **contraception** or treatment and/or prevention of secondary amenorrhea, dysfunctional bleeding, uterine leiomyomata, endometriosis, polycystic ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon, prostate or minimization of side effects or cyclic menstrual bleeding. Additional uses include stimulation of food intake.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-A02; B06-D02; B06-D06; B14-H01; B14-N14; B14-P01B

TECH UPTX: 20010116

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The progestational agent is levonorgestrel, norgestrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, methindrone acetate, norgestimate, osaterone, cycloproterone acetate, trimegestone, dienogest, dropsirenone,  **nomegestrol** or (17-deacetyl)norgestimate

(especially levonorgestrel). The antiprogestin compound is selected from (9 compounds specified): 6-(3-chlorophenyl)-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one or its pharmaceutically acceptable salt; 6(3-chlorophenyl)-4-cyclopropyl-1H-quinazolin-2-one or its pharmaceutically acceptable salt. Preparation - The antiprogestin compounds are prepared e.g. by treating appropriately substituted ortho-amino benzoic acid or derivative (1) with suitable organometallic agent, e.g. Grignard reagent, in appropriate non protic solvent to provide ortho-amino carbinol (2). Arylation of the aminocarbinol using Suzuki and Stille reaction conditions in the presence of transition metal catalysts with phosphino ligands or Pd-acetate with appropriately substituted nucleophilic agent such as aryl boronic acid, arylstannane etc to give compound (3). The compounds of the invention can be prepared from the carbinol 3 by reacting with appropriate ketone in the presence of suitable acid catalyst such as p-toluene sulfonic acid.

L121 ANSWER 9 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD  
 AN 2001-024741 [03] WPIX  
 DNC C2001-007493  
 TI Method of **contraception** comprises administration of progestational agent, antiprogestin and optionally placebo over 28 day cycle.  
 DC B01 B02  
 IN COLLINS, M A; EDWARDS, J P; GRUBB, G S; JONES, T K; MACKNER, V A; TEGLEY, C M; WROBEL, J E; ZHI, L; MARSCHKE, K B  
 PA (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC  
 CYC 93  
 PI WO 2000066163 A1 20001109 (200103)\* EN 43p A61K045-06  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2000046819 A 20001117 (200111) A61K045-06  
 US 6319912 B1 20011120 (200174) A61K031-56  
 EP 1173209 A1 20020123 (200214) EN A61K045-06  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI  
 ADT WO 2000066163 A1 WO 2000-US11642 20000501; AU 2000046819 A AU 2000-46819  
 20000501; US 6319912 B1 Provisional US 1999-183023P 19990504, US  
 2000-552038 20000419; EP 1173209 A1 EP 2000-928610 20000501, WO  
 2000-US11642 20000501  
 FDT AU 2000046819 A Based on WO 200066163; EP 1173209 A1 Based on WO 200066163  
 PRAI US 2000-552038 20000419; US 1999-183023P 19990504  
 IC ICM A61K031-56; A61K045-06  
 ICS A61K031-535; A61K031-57; A61P015-18  
 ICI A61K031:565; A61K031:425; A61K031-57  
 AB WO 200066163 A UPAB: 20011203  
 NOVELTY - **Contraceptive** regimen comprising separate administration of progestational agent and antiprogestin over 28 day cycle.  
 DETAILED DESCRIPTION - A method of **contraception** comprises administering:  
 (a) a first phase of 14-24 daily dosage units of a progestational agent equal in progestational activity to 35-100 micro g levonorgestrel;  
 (b) a second phase of 1-11 daily dosage units, at a daily dosage of 2-50 mg of an antiprogestin compound of formula (I) or its salt; and  
 (c) optionally a third phase of daily dosage units of an orally acceptable placebo for remaining days of the 28 consecutive days in which no antiprogestin, progestin or estrogen is administered;  
 to a female of child bearing age for 28 consecutive days. The total daily dosage units (a)-(c) equals 28.  
 R<sub>1</sub>, R<sub>2</sub> = H, optionally substituted alkyl, OH, optionally substituted alkoxy, aryl or heteroaryl; arylalkyl, heteroarylalkyl or alkynyl; or  
 R<sub>1</sub> + R<sub>2</sub> = -CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CMe<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -O(CH<sub>2</sub>)<sub>p</sub>CH<sub>2</sub>-,

$O(CH_2)_qO$ -,  $-CH_2CH_2OCH_2CH_2$ -,  $-CH_2CH_2NR_7CH_2CH_2$ -, or a double bond having two methyl groups, a cycloalkyl group, an oxygen bonded or a cycloether bonded to the terminal end;

$R_7$  = H or 1-6C alkyl;

$n$  = 1-5;

$p, q$  = 1-4;

$R_3$  = H, OH, NH<sub>2</sub>, COR<sub>a</sub>; optionally substituted alkyl; or alkenyl or alkynyl;

$R_a$  = H; or optionally substituted alkyl, alkoxy or aminoalkyl;

$R_4$  = H, halo, CN, NH<sub>2</sub>, optionally substituted alkyl, alkoxy, or optionally substituted aminoalkyl;

$R_5$  = phenyl substituted by X, Y and Z;

X = halo, OH, CN; optionally substituted alkyl, alkoxy, thioalkyl or aminoalkyl; S(O)alkyl, S(O)<sub>2</sub>alkyl, NO<sub>2</sub>, perfluoroalkyl, 5 or 6 membered heterocycle containing 1-3 heteroatoms, thioalkoxy, -COR<sub>b</sub>, -OCOR<sub>b</sub> or NR<sub>c</sub>COR<sub>b</sub>;

$R_b$  = H; or optionally substituted alkyl, aryl, alkoxy or aminoalkyl;

$R_c$  = H or optionally substituted alkyl;

Y, Z = H, halo, CN, NO<sub>2</sub>, alkoxy, alkyl or thioalkyl; or

$R_5$  = 5 or 6 membered heteroaryl containing 1-3 O, S, SO, SO<sub>2</sub> or NR<sub>6</sub> and optionally substituted on C by 1-2 H, halo, CN, NO<sub>2</sub>, alkyl, alkoxy, aminoalkyl, COR<sub>d</sub>, or NReCOR<sub>d</sub>;

$R_d$  = H, or optionally substituted alkyl, aryl, alkoxy or aminoalkyl;

$R_e$  = H or optionally substituted alkyl;

$R_6$  = H, alkyl, alkoxy carbonyl or is absent when the N or NR<sub>6</sub> is bonded to a ring double bond.

INDEPENDENT CLAIMS are included for:

(1) a method of **contraception** comprising administering to a female of child bearing age over a period of 28 consecutive days:

(a) a first phase of 18-21 daily dosage units of progestational agent equal in progestational activity to 35-150 micro g levonorgestrel and ethinyl **estradiol** at a daily dosage of 10-35 micro g;

(b) a second phase of 1-7 daily dosage units of an antiprogestin as above at a daily dose of 2-50 mg and optionally 10-35 micro g ethinyl **estradiol**; and

(c) optionally an orally acceptable placebo for each remaining day of the 28 consecutive days;

(2) kits comprising the **contraceptive** regimens as above.

ACTIVITY - Contraceptive; gynecological; cytostatic. No relevant activity example given

MECHANISM OF ACTION - Progestational; antiprogestational.

USE - The methods are useful for contraception (claimed) and for hormone replacement therapy, in the treatment of endometriosis, luteal phase defects, benign breast and prostatic diseases and prostatic, ovarian, breast, uterine and endometrial cancers.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-C05; B06-F01; B14-D01C; B14-D02A; B14-H01; B14-N07A; B14-N14;  
B14-P01B

TECH UPTX: 20010116

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Method: The progestational agent is levonorgestrel, norgestrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, norethindrone acetate, norgestimate, osaterone, cycloproterone acetate, trimegestone, dienogest, dropsirenone, **nomegestrol** or (17-deacetyl)norgestimate (especially levonorgestrel). The antiprogestin compound is 5-(3-chlorophenyl)-spiro(2,1-benzisothiazole-3(1H),1'-cyclohexane)2,2-dioxide or its pharmaceutically acceptable salt.

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AN 2001-007155 [01] WPIX

DNC C2001-001785

TI A method of **contraception** comprises administering substituted indoline derivatives useful also for e.g. the treatment and/or prevention of secondary amenorrhea and dysfunctional bleeding.

DC B01 B02  
 IN BENDER, R H W; EDWARDS, J P; GRUBB, G S; JONES, T K; MARSCHKE, K B;  
 TEGLEY, C M; WROBEL, J E; ZHANG, P; ZHI, L  
 PA (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC  
 CYC 93  
 PI WO 2000066168 A1 20001109 (200101)\* EN 86p A61K045-06  
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
 OA PT SD SE SL SZ TZ UG ZW  
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
 AU 2000049801 A 20001117 (200111) A61K045-06  
 EP 1173213 A1 20020123 (200214) EN A61K045-06  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI  
 ADT WO 2000066168 A1 WO 2000-US11845 20000501; AU 2000049801 A AU 2000-49801  
 20000501; EP 1173213 A1 EP 2000-932006 20000501, WO 2000-US11845 20000501  
 FDT AU 2000049801 A Based on WO 200066168; EP 1173213 A1 Based on WO 200066168  
 PRAI US 2000-552355 20000419; US 1999-198249 19990504  
 IC ICM A61K045-06  
 ICS A61K031-57; A61P015-18  
 ICI A61K031:565; A61K031:565; A61K031:565; A61K031:565; A61K031:54;  
 A61K031:535; A61K031:495; A61K031:41; A61K031-57; A61K031-57;  
 A61K031-57; A61K031-57  
 AB WO 200066168 A UPAB: 20001230  
 NOVELTY - A method of **contraception** which comprises  
 administering to a female of child bearing age substituted indoline  
 derivatives (I) over 28 consecutive days.  
 DETAILED DESCRIPTION - A method of **contraception** which  
 comprises administering to a female of child bearing age for 28  
 consecutive days: (a) a first phase of 14-24 daily dosage units of a  
 progestational agent equal in progestational activity to 35-100 micro g  
 levonorgestrel; (b) a second phase of 1-11 daily dosage units, at a daily  
 dosage of 2-50 mg, of an antiprogestin compound of formula (I) or its  
 salt; and optionally (c) a third phase of daily dosage units of a placebo  
 for the remaining days of the 28 consecutive days in which no  
 antiprogestin, progestin or **estrogen** is administered and the  
 total daily dosage units of the first, second and third phases equals 28:  
 A = O, S or NR4;  
 B = bond between A and C=Q, or CR5R6;  
 R4, R5, R6 = H, optionally substituted 1-6C alkyl, optionally  
 substituted 2-6C alkenyl, optionally substituted 2-6C alkynyl, optionally  
 substituted 3-8C cycloalkyl, optionally substituted aryl, optionally  
 substituted heterocyclic or cyclic alkyl constructed by fusing R4 and R5  
 to form a 5-7 membered ring;  
 R1 = H, OH, NH2, optionally substituted 1-6C alkyl, 3-6C alkenyl,  
 substituted 1-6C alkenyl, optionally substituted alkynyl or CORA;  
 RA = H, optionally substituted 1-3C alkyl, optionally substituted  
 aryl, optionally substituted 1-3C alkoxy or optionally substituted 1-3C  
 aminoalkyl;  
 R2 = H, halo, CN, NO2, optionally substituted 1-6C alkyl, optionally  
 substituted 1-6C alkoxy or optionally substituted 1-6C aminoalkyl;  
 R3 = a or b;  
 a = benzene ring trisubstituted by X, Y or Z;  
 X = halo, CN, optionally substituted 1-3C alkyl, optionally  
 substituted 1-3C alkoxy, optionally substituted 1-3C thioalkoxy,  
 optionally substituted 1-3C aminoalkyl, NO2, 1-3C perfluoroalkyl, 5 or 6  
 membered heterocyclic ring containing 1-3 heteroatoms, CORB, OCORB or  
 NRCCORB;  
 RB = H, optionally substituted 1-3C alkyl, optionally substituted  
 aryl, optionally substituted 1-3C alkoxy or optionally substituted 1-3C  
 aminoalkyl;  
 RC = H or optionally substituted 1-3C alkyl;  
 Y, Z = H, halo, CN, NO2, 1-3C alkoxy, 1-3C alkyl or 1-3C thioalkoxy;  
 b = 5 or 6 membered ring with 1,2 or 3 heteroatoms from O, S, SO, SO2

or NR7 and containing 1 or 2 substituents from H, halo, CN, NO2, 1-3C alkyl, 1-3C alkoxy, 1-3C aminoalkyl, CORD or NRECORD;

RD = H, optionally substituted 1-3C alkyl, optionally substituted aryl, optionally substituted 1-3C alkoxy or optionally substituted 1-3C aminoalkyl;

RE = H or optionally substituted 1-3C alkyl; and

R7 = H or 1-3C alkyl.

INDEPENDENT CLAIMS are also included for the following:

(i) a method as above where the progestational agent is levonorgestrel and the antiprogestin is a compound of formula (II) or its salt;

(ii) a method of **contraception** which comprises administering to a female of child bearing age over a period of 28 consecutive days: (a) a first phase of 18-21 daily dosage units of progestational agent equal in progestational activity to 35-150 micro g levonorgestrel and ethinyl **estradiol** at a daily dose range of from 10-35 micro g; (b) a second phase of 1-7 daily dosage units of an antiprogestin (I) at a daily dose of 2-50 mg; and optionally (c) a placebo for each remaining day of the 28 consecutive days;

(iii) as in method (ii) except second phase is 1-7 daily dosage units, each daily dose unit containing an antiprogestin (I) at a concentration of 2-50 mg and ethinyl **estradiol** at a concentration of 10-35 micro g;

(iv) a kit adapted for oral administration over a 28 day period which comprises: (a) a first phase of 14-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 micro g levonorgestrel; (b) a second phase of 1-11 daily dosage units of an antiprogestin (I) at a daily dosage of 2-50 mg; and (c) a third phase of daily dosage units of a placebo;

(v) a kit adapted for oral administration over a 28 day period which comprises: (a) a first phase of 18-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 micro g levonorgestrel and ethinyl **estradiol** at a daily dose of 10-35 micro g; (b) a second phase of 1-7 daily dosage units of an antiprogestin (I) at a daily dosage of 2-50 mg; and (c) a third phase of daily dosage units of a placebo; and

(vi) a kit adapted for oral administration over a 28 day period which comprises: (a) a first phase of 18-21 daily dosage units of a progestational agent equal in progestational activity to 35-150 micro g levonorgestrel and ethinyl **estradiol** at a daily dose of 10-35 micro g; (b) a second phase of 1-7 daily dosage units of an antiprogestin (I) at a daily dosage of 2-50 mg and ethinyl **estradiol** at a concentration of 10-35 micro g; and (c) a third phase of from 0-9 daily dosage units of a placebo.

R1' = H, OH, NH2, optionally substituted 1-6C alkyl or CORA;

RA' = H, 1-4C alkyl or 1-4C alkoxy;

R2' = H, halo, CN, NO2 or optionally substituted 1-3C alkyl;

R3' = benzene disubstituted by X' at the 3' position and by Y' on 4' or 5' position;

X' = halo, CN, 1-3C alkoxy, 1-3C alkyl, NO2, 1-3C perfluoroalkyl, 5 membered heterocyclic ring containing 1-3 heteroatoms or 1-3C thioalkoxy; and

Y' = H, halo, CN, NO2, 1-3C alkoxy, 1-4C alkyl or 1-3C thioalkoxy.

ACTIVITY - Contraceptive; gynecological; cytostatic; anabolic.

MECHANISM OF ACTION - Progesterone receptor antagonists.

The compounds of the invention were tested in assays and their potency in the range of 0.01 nM to 5 mM in the *vitro* assays and 0.001-300 mg/kg in the *in vivo* assays. For one compound a IC50 (nM) hPR CV-1 of 147 was obtained.

USE - These regimens and combinations may be administered to a mammal to induce contraception or for the treatment and/or prevention of secondary amenorrhea, dysfunctional bleeding, uterine leiomyomata, endometriosis, polycystic ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon, prostate. Additional uses include the stimulation of food intake.

FS CPI  
 FA AB; GI; DCN  
 MC CPI: B01-A02; B01-C04; B01-C05; B01-C06; B01-C09; B06-H; B14-D01B;  
     B14-F08; B14-H01; B14-N14; B14-P01B  
 TECH UPTX: 20001230  
 TECHNOLOGY FOCUS - PHARMACEUTICALS - The progestational agent is selected from levonorgestrel, norgetrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, norethindrone acetate, norgestimate, osaterone, cyproterone acetate, trimegestone, dienogest, drospirenone, **nomegestrol** or (17-deacetyl)norgestimate.

L121 ANSWER 11 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD  
 AN 2000-679728 [66] WPIX  
 DNC C2000-206816  
 TI **Contraception** method for cyclic combination therapy comprise indoline derivatives and progestational agents.  
 DC B01 B02  
 IN BENDER, R H W; EDWARDS, J P; FENSONE, A; GRUBB, G S; JONES, T K; MILLER, L L; TEGLEY, C M; ULLRICH, J W; WROBEL, J E; ZHANG, P; ZHI, L  
 PA (AMHP) AMERICAN HOME PROD CORP; (LIGA-N) LIGAND PHARM INC  
 CYC 93  
 PI WO 2000066167 A1 20001109 (200066)\* EN 135p A61K045-06  
     RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL  
     OA PT SD SE SL SZ TZ UG ZW  
     W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ  
     EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK  
     LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI  
     SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
     AU 2000048139 A 20001117 (200111) A61K045-06  
     EP 1173212 A1 20020123 (200214) EN A61K045-06  
     R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
     RO SE SI  
 ADT WO 2000066167 A1 WO 2000-US11834 20000501; AU 2000048139 A AU 2000-48139  
     20000501; EP 1173212 A1 EP 2000-930287 20000501, WO 2000-US11834 20000501  
 FDT AU 2000048139 A Based on WO 200066167; EP 1173212 A1 Based on WO 200066167  
 PRAI US 2000-552358 20000419; US 1999-183052 19990504  
 IC ICM A61K045-06  
     ICS A61K031-40; A61K031-565; A61P015-18  
 ICA A61K031-57  
 ICI A61K031:40, A61K031:565, A61K031:57; A61K031-40, A61K031:565  
 AB WO 200066167 A UPAB: 20001219  
 NOVELTY - Method of **contraception** comprises administering a first phase of 14-24 daily dosage units of a progestational agent, a second phase of 1-11 daily dosage units of an antiprogestin (I) over 28 days, and optionally a third phase comprising administering a placebo.  
 DETAILED DESCRIPTION - Method of **contraception** comprises administering to a woman of child bearing age for 28 consecutive days a first phase of 14-24 daily dosage units of a progestational agent equal in progestational activity to 35-100 micro g levonorgestrel, a second phase of 1-11 daily dosage units of 2-50 mg/day of an antiprogestin of formula (I) or its salts, and optionally a third phase comprising a placebo, where total daily dosage units of the phases equals 28.  
 R<sub>1</sub>, R<sub>2</sub> = alkyl, alkoxy, aryl or heteroaryl (all optionally substituted), H, OH, OAc, arylalkyl, alkylheteroaryl, 1-propynyl or 3-propynyl; or  
 R<sub>1</sub> + R<sub>2</sub> = a ring comprising -CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CMe<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -O(CH<sub>2</sub>)<sub>m</sub>CH<sub>2</sub>-, -O(CH<sub>2</sub>)<sub>p</sub>O-, -CH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>N(H or alkyl)CH<sub>2</sub>CH<sub>2</sub>-; or  
 R<sub>1</sub> + R<sub>2</sub> = double bond to CMe<sub>2</sub>, C(cycloalkyl), O or C(cycloether);  
 n = 0-5;  
 m = 1-4;  
 p = 1-4;  
 R<sub>3</sub> = 1-6C alkyl, 3-6C alkenyl or alkynyl (all optionally substituted), H, OH, NH<sub>2</sub> or CORa;  
 Ra = 1-3C alkyl, 1-3C alkoxy, 1-3C or 1-3C aminoalkyl (all optionally substituted) or H;

R4 = 1-6C alkyl, 1-6C alkoxy or 1-6C aminoalkyl (all optionally substituted), H, NH2, CN or halo;

R5 = phenyl substituted by X, Y and Z, a 5-6 membered heterocycle with 1-3 NR6, O, S, SO2 or SO, and 1-2 W, or indol-4-yl, indol-7-yl or benzo-2-thiophene (optionally substituted with 1-3 halo, lower alkyl, CN, NO2, lower alkoxy or CF3);

X = 1-3C alkyl, 1-3C alkoxy, 1-3C thioalkyl or 1-3C aminoalkyl (all optionally substituted), halo, OH, CN, S(O)alkyl, S(O)2alkyl, NO2, a 5-6 membered heterocyclic ring containing 1-3 heteroatoms, CORb, OCORb or NRcCORb;

Y, Z = H, halo, CN, NO2, 1-3C alkyl, 1-3C alkoxy or 1-3C thioalkyl;  
W = H, halo, CN, NO2, 1-3C alkyl, 1-3C alkoxy or 1-3C aminoalkyl,

CORD or NReCORD;

R6 = H or 1-3C alkyl;

Rb, Rd = 1-3C alkyl, aryl, 1-3C alkoxy or 1-3C aminoalkyl (all optionally substituted) or H; and

Rc, Re = H or 1-3C alkyl (optionally substituted).

An INDEPENDENT CLAIM is included for a kit comprising 18-21 daily doses of levonorgestrel (35-100 micro g/day) and ethinyl estradiol (10-35 micro g/day), 1-7 daily doses of (I) (2-50 mg/day) and ethinyl estradiol (10-35 micro g/day) and daily placebos (up to 28 daily dosage units).

ACTIVITY - **Contraceptive; gynecological; cytostatic; anabolic.**

MECHANISM OF ACTION - Progesterone receptor antagonist.

In a rat deciduation assay, Ki (nM) and IC50 (nM) values against CV-1 cells for 5-(3-fluoro-5-nitrophenyl)spiro(cyclohexane-1,3-(3H)indol-2(1H)-one (I') were 9 and 1 respectively, with a decidual response of 60% at 10 mg/kg.

USE - As a method for **contraception** for females of child bearing age (claimed). The method may also be used for treatment of secondary amenorrhea, dysfunctional bleeding, uterine leiomyomata, endometriosis, polycystic ovary syndrome, carcinomas and adenocarcinomas of the endometrium, ovary, breast, colon or prostate, minimization of side effects or cyclic menstrual bleeding, and for stimulation of food intake.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B01-A02; B01-C03; B01-C04; B01-C05; B01-C09; B06-B01; B06-D01;  
B12-M11; B14-D02A; B14-E11; B14-H01B; B14-N07A; B14-N14;  
**B14-P01B**

TECH UPTX: 20001219

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preparation: No suitable preparation given.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Active Agent: The progestational agent is levonorgestrel (preferred), norgestrel, desogestrel, 3-ketodesogestrel, norethindrone, gestodene, norethindrone acetate, norgestimate, cyproterone acetate, trimegestone, dienogest, drospirenone, **nomegestrol** or (17-acetyl)norgestimate.

L121 ANSWER 12 OF 12 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1997-145360 [13] WPIX

DNC C1997-046372

TI Oral treatment of **oestrogen** deficiency in menopausal women - by sequential admin. of dosage units contg. **oestrogen** only, **oestrogen** plus **progestagen** and placebo to re-establish the endometrial cycle.

DC B01

IN LANQUETIN, M; PARIS, J; THOMAS, J L; THOMAS, J  
PA (SOTH) THERAMEX LAB SA

CYC 41

PI WO 9704784 A1 19970213 (199713)\* FR 20p A61K031-57

RW: AT BE CH DE DK ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE  
SZ UG

W: AU BR CA CN CZ FI HU IL JP KR MX NO RU SG US VN

FR 2737411 A1 19970207 (199715) 16p A61K031-57  
 AU 9663674 A 19970226 (199725) A61K031-57  
 NO 9701449 A 19970530 (199732) A61K000-00  
 EP 783310 A1 19970716 (199733) FR A61K031-57  
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE  
 ZA 9606545 A 19970730 (199735) 17p A61K000-00  
 BR 9606549 A 19980623 (199832) A61K031-57  
 JP 10507207 W 19980714 (199838) 17p A61K031-565  
 CZ 9700967 A3 19980812 (199839) A61K031-57  
 KR 97706004 A 19971103 (199844) A61K031-57  
 US 5891867 A 19990406 (199921) A61K031-56  
 HU 9900612 A2 19990728 (199936) A61K031-57  
 MX 9702381 A1 19980201 (199954) A61K031-57  
 AU 722355 B 20000727 (200041) A61K031-57  
 CN 1167438 A 19971210 (200165) A61K031-57  
 ADT WO 9704784 A1 WO 1996-IB754 19960729; FR 2737411 A1 FR 1995-9364 19950801;  
 AU 9663674 A AU 1996-63674 19960729; NO 9701449 A WO 1996-IB754 19960729,  
 NO 1997-1449 19970326; EP 783310 A1 EP 1996-923018 19960729, WO 1996-IB754  
 19960729; ZA 9606545 A ZA 1996-6545 19960801; BR 9606549 A BR 1996-6549  
 19960729, WO 1996-IB754 19960729; JP 10507207 W WO 1996-IB754 19960729, JP  
 1997-507406 19960729; CZ 9700967 A3 WO 1996-IB754 19960729, CZ 1997-967  
 19960729; KR 97706004 A WO 1996-IB754 19960729, KR 1997-702125 19970401;  
 US 5891867 A WO 1996-IB754 19960729, US 1997-817329 19970424; HU 9900612  
 A2 WO 1996-IB754 19960729, HU 1999-612 19960729; MX 9702381 A1 MX  
 1997-2381 19970401; AU 722355 B AU 1996-63674 19960729; CN 1167438 A CN  
 1996-191100 19960729  
 FDT AU 9663674 A Based on WO 9704784; EP 783310 A1 Based on WO 9704784; BR  
 9606549 A Based on WO 9704784; JP 10507207 W Based on WO 9704784; CZ  
 9700967 A3 Based on WO 9704784; KR 97706004 A Based on WO 9704784; US  
 5891867 A Based on WO 9704784; HU 9900612 A2 Based on WO 9704784; AU  
 722355 B Previous Publ. AU 9663674, Based on WO 9704784  
 PRAI FR 1995-9364 19950801  
 REP 2.Jnl.Ref; DE 3229612; WO 9406437  
 IC ICM A61K000-00; A61K031-56; A61K031-565; A61K031-57  
 ICS A61K009-20  
 ICI A61K031-57, A61K031:565; A61K031-57, A61K031:565; A61K031-57, A61K031:565  
 AB WO 9704784 A UPAB: 19970326  
*Oestrogen* deficiency in menopausal women is treated by oral  
 admin., during the whole of the month, of, in sequence, (a)  
*oestrogen* (I) only; (b) (I) plus a *progestagen* (II) and  
 (c) a placebo.  
 USE - The treatment is used to compensate functional disorders  
 characteristic of (post)menopausal hypo-*oestrogenism*, esp. to  
 re-establish the endometrial cycle and to reduce the number of hot  
 flushes. The treatment also slows down post-menopausal bone restructuring,  
 so may prevent osteoporosis.  
 Dwg:0/0  
 FS CPI  
 FA AB; DCN  
 MC CPI: B04-J02; B14-N14

=> d his

(FILE 'HOME' ENTERED AT 13:42:22 ON 15 MAR 2002)  
 SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:42:43 ON 15 MAR 2002

L1 1 S NOMEGESTROL/CN  
 L2 1 S NOMEGESTROL ACETATE/CN  
 L3 1 S ESTRADIOL/CN

FILE 'EMBASE' ENTERED AT 13:43:28 ON 15 MAR 2002

L4 263 S L1 OR L2  
 L5 267 S NOMEGESTROL OR NOMEGESTROL ACETATE  
 L6 151 S TX071 OR TX066 OR TX()(071 OR 066) OR LUTENYL OR UNIPLANT

L7 267 S L4-L6  
 L8 42996 S L3  
 L9 60794 S ESTRADIOL  
 L10 60794 S L8,L9  
 L11 67578 S GESTAGEN+NT/CT  
     E PROGESTAGEN/CT  
     E E3+ALL  
 L12 67579 S L7,L11  
 L13 93648 S ESTROGEN+NT/CT  
     E SYNTHETIC/CT  
 L14 102037 S L10,L13  
 L15 38896 S L12 AND L14  
 L16 216929 S DRUG COMBINATION+NT/CT  
 L17 6314 S L15 AND L16  
 L18 37 S L5/CT (L) CB/CT  
 L19 1774 S L9/CT (L) CB/CT  
 L20 24 S L18 AND L19  
 L21 24 S L20 AND L15,L17  
 L22 51142 S CONTRACEPTION+NT/CT  
 L23 8046 S L22 AND L15  
 L24 5 S L23 AND L21  
 L25 2 S L24 AND CONTRACEPT?/TI,BI,CT  
 L26 1517 S L17 AND L23  
 L27 182 S L23 AND L18,L19  
 L28 1517 S L26,L27  
     E CONTRACEPTION/CT  
     E E3+ALL  
 L29 21785 S E4 OR E12 OR E30 OR E31 OR E32 OR E33 OR E34 OR E35 OR E36 OR  
 L30 1122 S L29 AND L28  
 L31 13 S L30 AND L7  
 L32 346 S L30 AND L10  
 L33 7 S L32 AND L31  
 L34 71 S L29 AND L7  
 L35 19 S L34 AND L10  
 L36 16 S L35 AND PY<=1999  
     SEL DN 9 12  
 L37 2 S L36 AND E1-E2  
 L38 2 S L25,L37  
     E OVULATION/CT  
     E E3+ALL  
 L39 8341 S E1  
     E OVULATION/CT  
     E E6+AKK  
     E E3+ALL  
 L40 870 S E2+NT  
 L41 1673 S L39,L40 AND L15  
 L42 11 S L41 AND L7  
 L43 99 S L7 AND L9/CT  
 L44 10 S L43 AND L29  
 L45 5 S L43 AND L39,L40  
 L46 12 S L44,L45  
     E ESTRADIOL/CT  
     E ESTRADIOL PLUS/CT  
 L47 68 S ESTRADIOL PLUS?/CT AND L17-L21  
 L48 1596 S L17-L21 AND PLUS NOT L47  
 L49 16 S L48 AND L7  
 L50 2 S L38 AND L4-L49

FILE 'EMBASE' ENTERED AT 14:15:38 ON 15 MAR 2002

L51 6263 S L11 (L) CB/CT  
 L52 70 S L7 AND L51  
 L53 32 S L52 AND L19  
 L54 2 S L53 AND (CONTRACEP? OR OVULAT? OR BIRTH(L)CONTROL? OR PREGNAN  
 L55 0 S L54 NOT L50

FILE 'MEDLINE' ENTERED AT 14:17:43 ON 15 MAR 2002

L56 98 S L7  
 L57 66096 S L10  
 L58 45 S L56 AND L57  
     SEL DN AN 16 38 39  
 L59 3 S L58 AND E1-E9  
 L60 11 S L58 AND CONTRACEP?  
 L61 3 S L60 AND L59  
 L62 8 S L60 NOT L61  
     E CONTRACEPT/CT  
 L63 0 S E4+NT AND L58  
 L64 42 S E44+NT AND L58  
 L65 42 S E46+NT AND L58  
 L66 0 S E124+NT AND L58  
 L67 0 S E125+NT AND L58  
 L68 42 S E198+NT AND L58  
 L69 4 S E199+NT AND L58  
 L70 38 S E222+NT AND L58  
 L71 2 S E246+NT AND L58  
 L72 15 S E259+NT AND L58  
 L73 1 S E310+NT AND L58  
 L74 1 S E326+NT AND L58  
 L75 42 S L64-L74  
 L76 19 S L75 AND COMBIN?  
 L77 16 S L75 AND (COADMINT? OR COMED? OR COPRESCRI? OR COTHERAP? OR PL  
 L78 24 S L76, L77  
 L79 9 S L78 NOT ?MENOPAUS?  
     SEL DN 2 4 6 7 8 AN  
 L80 5 S L79 AND E1-E15  
 L81 5 S L61, L80 AND L56-L80  
 L82 1 S L58 AND COADMIN?  
 L83 5 S L81, L82

FILE 'MEDLINE' ENTERED AT 14:33:39 ON 15 MAR 2002

FILE 'WPIX' ENTERED AT 14:33:54 ON 15 MAR 2002

L84 15 S L5, L6  
 L85 563 S ?GESTAGEN?  
 L86 5048 S ?ESTRADIOL? OR ?ESTROG?  
     E NOMEGESTROL/DCN  
     E ESTRADIOL/DCN  
     E E3+ALL  
 L87 877 S E2 OR 0014/DRN  
 L88 4 S E4  
 L89 70 S E6 OR 0024/DRN  
 L90 15 S E8  
 L91 8 S E10  
 L92 80 S E12  
 L93 60 S E16  
 L94 3 S E18  
 L95 2 S E20  
 L96 194 S E24 OR 0013/DRN  
 L97 6 S E26  
 L98 2 S E28  
 L99 216 S E32 OR 0069/DRN  
 L100 4 S E34  
 L101 23 S E36  
 L102 26 S E38  
 L103 1 S E40  
 L104 259 S L84, L85 AND L86-L103  
 L105 52 S L104 AND (P841 OR P841 OR P843 OR P840)/M0, M1, M2, M3, M4, M5, M6  
 L106 111 S (B12-K03 OR C12-K03 OR B14-P01 OR C14-P01 OR B14-P01B OR C14-  
 L107 13 S L104, L106 AND L84  
     E PARIS J/AU  
 L108 95 S E3-E10  
     E THOMAS J/AU  
 L109 220 S E3, E17, E18

L110 5 S L108,L109 AND L104  
E THERAMEX/PA  
L111 5 S E3,E4,E5 AND L104  
L112 5 S L110,L111  
L113 4 S L107 AND L112  
L114 5 S L112,L113  
L115 9 S L107 NOT L114  
L116 7 S L115 NOT (DEHYDROGENASE OR TESTOSTERONE)/TI  
L117 9 S L114,L116 AND ?CONTRACEP?  
L118 2 S L114,L116 AND OVUL?  
L119 9 S L117,L118  
L120 3 S L114,L116 NOT L119  
L121 12 S L119,L120 AND L84-L120

FILE 'WPIX' ENTERED AT 14:42:35 ON 15 MAR 2002

=> d his

(FILE 'HOME' ENTERED AT 11:04:48 ON 15 MAR 2002)  
SET COST OFF

FILE 'REGISTRY' ENTERED AT 11:05:07 ON 15 MAR 2002  
E NOMEGESTROL/CN  
L1 1 S E3  
L2 1 S E4  
L3 2 S L1,L2  
SEL RN  
L4 0 S E1-E2/CRN  
E ESTRADIOL/CN  
L5 1 S E3  
SEL RN  
L6 135 S E1/CRN

Jan Delaval  
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jan.delaval@uspto.gov

FILE 'HCAPLUS' ENTERED AT 11:06:59 ON 15 MAR 2002  
L7 79 S L3  
L8 85 S NOMEGESTROL OR NOMEGESTROL ACETATE OR TX071 OR TX066 OR TX() (L  
L9 94 S L7,L8  
L10 730 S GESTAGEN  
L11 10 S NORPREGNA(L)DIENE(L)DIONE(L)METHYL(L)(HYDROXY OR ACETOXY)(L  
L12 12 S NORPREGNA(L)DIENE(L)DIONE(L)METHYL(L)(HYDROXY OR ACETOXY)(L)1  
L13 12 S L11,L12  
L14 1 S L13 AND L9  
L15 94 S L9,L14  
L16 886 S GESTAGEN?  
L17 886 S L10,L16  
L18 43509 S L5  
L19 642 S L6  
L20 62702 S ESTRADIOL  
L21 72884 S ?ESTROGEN?  
E ESTROGEN/CT  
E E33+ALL  
L22 33184 S E7,E6+NT  
L23 37 S L15 AND L18,L19,L20  
L24 484 S L15,L17 AND L18-L22  
L25 8 S CONTRACEPT? AND L23  
L26 164 S CONTRACEPT? AND L24  
L27 164 S L25,L26  
L28 92 S L23,L24 AND (OVULAT? OR OVARY)  
L29 78 S L23,L24 AND OVARIAN  
E CONTRACEPT/CT  
E E7+ALL  
L30 117 S E4+NT AND L23,L24  
L31 5 S E8+NT AND L23,L24  
E E8+ALL  
L32 73 S E2+NT AND L23,L24  
L33 21 S (FERTIL? OR INFERTIL?) AND L23,L24  
L34 256 S L27-L33  
E ORAL CONTRACEPTIVE/CT  
E E4+ALL  
L35 59 S E1,E2 AND L23,L24  
E OVAR/CT  
E E15+ALL  
L36 56 S E3+NT AND L23,L24  
L37 4 S E16+NT AND L23,L24  
L38 0 S E18+NT AND L23,L24  
L39 1 S E21+NT AND L23,L24  
E OVAR/CT  
E E29+ALL  
L40 .5 S E1,E2 AND L23,L24  
L41 259 S L34-L40  
L42 456 S L23,L24 AND (PD<=19991025 OR PRD<=19991025 OR AD<=19991025)  
E PARIS J/AU

L43 17 S E3-E16 AND L23,L24  
       E THOMAS J/AU  
 L44 1 S E3,E4,E38,E39 AND L23,L24  
       E THOMAS JEAN/AU  
 L45 7 S E3,E12,E14 AND L23,L24  
 L46 18 S L43-L45 AND L42  
 L47 3 S L41 AND L46  
       E THERAMEX/PA,CS  
 L48 13 S L23,L24 AND E3-E8  
 L49 12 S L48 AND L42  
 L50 3 S L49 AND L41  
 L51 4 S L47,L50  
 L52 2 S L51 AND (COMPOSITION OR MEDICINE)/TI  
 L53 15 S L46,L49 NOT L51-L52  
       SEL DN 1 2 4 5 6 14  
 L54 6 S L53 AND E1-E6  
 L55 8 S L52,L54  
 L56 272 S L23,L24 AND (COADMIN? OR COMEDIC? OR COPREScri? OR COTHERAP?  
 L57 24 S L56 AND COMPOSITION/CW  
 L58 248 S L56 NOT L57  
 L59 24 S L58 AND L9  
 L60 19 S L59 AND L18,L20  
 L61 5 S L59 NOT L60  
       SEL DN 2 3  
 L62 2 S L61 AND E7-E8  
 L63 10 S L55,L62  
 L64 13 S L60 NOT L63  
 L65 7 S L63,L64 AND ?CONTRACEPT?  
 L66 164 S L23,L24 AND ?CONTRACEPT?  
 L67 10 S L66 AND L9  
 L68 9 S L67 NOT CRYST?/TI  
 L69 10 S L65,L68  
 L70 16 S L63,L64 NOT L69  
 L71 9 S L70 AND (PARIS ? OR THOMAS ?)/AU  
 L72 5 S L70 AND THERAMEX/PA,CS  
 L73 19 S L69,L71,L72  
 L74 15 S L73 NOT (CRYST? OR ULTRASOUND OR UREA OR OXOSPIRO)/TI  
 L75 4 S L73 NOT L74

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:55:09 ON 15 MAR 2002  
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FILE COVERS 1907 - 15 Mar 2002 VOL 136 ISS 11  
 FILE LAST UPDATED: 13 Mar 2002 (20020313/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d 174 all tot

L74 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2001:903818 HCAPLUS  
 DN 136:15686  
 TI Starter kit for low dose oral **estrogen contraceptives**  
 IN Grubb, Gary S.  
 PA American Home Products Corporation, USA  
 SO PCT Int. Appl., 13 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K031-00  
 CC 2-3 (Mammalian Hormones)  
 Section cross-reference(s): 63  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001093848	A2	20011213	WO 2001-US18142	20010605
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2002010167	A1	20020124	US 2001-872250	20010601
	US 2000-210310	P	20000608		
AB	An oral <b>contraceptive</b> starter kit comprising at least two cycle packs of compns. contg. an <b>estrogen</b> and a progestin is described. The <b>contraceptive</b> kit helps to overcome or ameliorate the problem of breakthrough bleeding and spotting assocd. with lowest dose (15-20 .mu.g ethynodiol <b>estrogen</b> <b>contraceptives</b> . For example, a kit with three cycle packs contained: (cycle 1) levonorgestrel (LNG) 150 .mu.g and ethynodiol (EE) 30 .mu.g (21 days), (cycle 2) LNG 50 .mu.g and EE 30 .mu.g (6 days), LNG 75 .mu.g and EE 40 .mu.g (5 days), and LNG 125 .mu.g and EE 30 .mu.g (10 days), and (cycle 3) LNG 100 .mu.g and EE 20 .mu.g (21 days).				
ST	<b>estrogen progestin oral contraceptive kit</b>				
IT	Drug delivery systems (oral; starter kit for low dose oral <b>estrogen contraceptives</b> )				
IT	Estrogens Progestogens RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (starter kit for low dose oral <b>estrogen contraceptives</b> )				
IT	51-98-9, Norethindrone acetate 52-76-6, Lynestrenol 57-63-6, Ethynodiol 68-22-4, Norethindrone 68-23-5, Norethynodrel 71-58-9, Medroxyprogesterone acetate 297-76-7, Ethynodiol diacetate 427-51-0, Cyproterone acetate 595-33-5, Megestrol acetate 797-63-7, Levonorgestrel 6533-00-2, Norgestrel 35189-28-7, Norgestimate 53016-31-2, 17-Deacetyl norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 58691-88-6, Nomegestrol 60282-87-3, Gestodene 67392-87-4, Drospirenone 74513-62-5,				

Trimegestone 105149-04-0, Osaterone  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (starter kit for low dose oral **estrogen**  
**contraceptives**)

L74 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2001:319731 HCAPLUS  
 DN 134:316160  
 TI Hormonal composition based on a progestational agent and an **estrogen**  
 IN Paris, Jacques; Thomas, Jean-louis  
 PA Laboratoire Theramex, Monaco  
 SO PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA French  
 IC ICM A61K031-57  
 ICS A61P005-30  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001030356	A1	20010503	WO 1999-FR2588	19991025 <-- RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
	WO 2001030357	A1	20010503	WO 2000-FR2939	20001024 <-- W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI	WO 1999-FR2588	W	19991025 <--		
AB	The invention concerns the field of therapeutic chem. and more particularly the field of hormonal pharmaceuticals technique. More precisely, it concerns novel hormonal compns. formed by an progestogen- <b>estrogen</b> combination consisting of an <b>estrogen</b> compd. and a progestational compd., assocd. or mixed with one or several pharmaceutically acceptable inert non-toxic carriers designed for oral administration. The invention also concerns the use of the progestogen- <b>estrogen</b> mixt. wherein the <b>estrogen</b> constituent and the progestogen constituent are administered in combination. The combined assocn. can be prescribed continuously or intermittently, so as to produce a compn. for treating <b>estrogen</b> deficiencies, preventing osteoporosis and cardiovascular diseases in postmenopausal women. The invention further concerns a method for prep. said novel pharmaceutical progestogen- <b>estrogen</b> compns. A tablet contained <b>estradiol</b> 0.811, <b> nomegestrol acetate</b> 0.338, lactose 71.238, cellulose 15.032, povidone 7.297, Precirol AT05 1.503, colloidal silica 0.540, and crospovidone 3.243%. Antimitotic effects of the compn. in endometrial cells was studied.				
ST	hormone progestational agent <b>estrogen</b> ; tablet <b>estradiol nomegestrol acetate</b> antimimetic				
IT	<b>Estrogens</b> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (conjugated; hormonal compn. based on progestational agent and <b>estrogen</b> )				
IT	Cardiovascular system (disease; hormonal compn. based on progestational agent and <b>estrogen</b> )				

IT Menopause  
 (hormonal compn. based on progestational agent and **estrogen**)

IT **Estrogens**  
 Hormones, animal, biological studies  
 Progestogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hormonal compn. based on progestational agent and **estrogen**)

IT Mitosis  
 (inhibitors; hormonal compn. based on progestational agent and **estrogen**)

IT Drug delivery systems  
 (tablets; hormonal compn. based on progestational agent and **estrogen**)

IT Osteoporosis  
 (therapeutic agents; hormonal compn. based on progestational agent and **estrogen**)

IT Drug delivery systems  
 (unit doses; hormonal compn. based on progestational agent and **estrogen**)

IT 50-28-2, **Estradiol**, biological studies 472-54-8,  
 19-Norprogesterone 979-32-8, **Estradiol** valerate  
**58652-20-3, Nomegestrol acetate**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hormonal compn. based on progestational agent and **estrogen**)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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 (2) Laboratoire Theramex; FR 2754179 A 1998 HCPLUS  
 (3) Plunkett, E; EP 0136011 A 1985 HCPLUS

L74 ANSWER 3 OF 15 HCPLUS COPYRIGHT 2002 ACS

AN 2001:319730 HCPLUS

DN 134:316159

TI **Contraceptive medicine** based on a progestational agent and an **estrogen**

IN Paris, Jacques; Thomas, Jean-louis

PA Laboratoire Theramex, Monaco

SO PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM A61K031-57

ICS A61P005-30

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001030355	A1	20010503	WO 1999-FR2587	19991025 <--
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	WO 2001030358	A1	20010503	WO 2000-FR2952	20001024 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	PRAI WO 1999-FR2587	W	19991025		<--

AB The invention concerns the field of chem. and more particularly the field of therapeutic chem. More particularly, it concerns novel contraceptive compns. consisting of a progestational agent and an estrogen. It specifically concerns novel pharmaceutical contraceptive compns. characterized in that they contain as active principles a nomegestrol and estradiol ester combined or mixed with a pharmaceutically acceptable inert non-toxic carrier or support suited for oral administration. A tablet contained 2.5% estradiol premixt. 44.45, nomegestrol acetate 0.33, colloidal silica 0.55, Crospovidone 3.60, lactose 28.89, microcryst. cellulose 19.18, stearic acid 2.00, and talc 1.00%. Antigonadotropic efficacy of the combination was studied in female volunteers.

ST oral contraceptive progestational agent estrogen; estradiol nomegestrol acetate tablet oral contraceptive

IT Drug delivery systems (capsules; contraceptive medicine based on progestational agent and estrogen)

IT Lubricants (contraceptive medicine based on progestational agent and estrogen)

IT Estrogens Progestogens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(contraceptive medicine based on progestational agent and estrogen)

IT Contraceptives (oral; contraceptive medicine based on progestational agent and estrogen)

IT Drug delivery systems (powders; contraceptive medicine based on progestational agent and estrogen)

IT Drug delivery systems (sachets; contraceptive medicine based on progestational agent and estrogen)

IT Drug delivery systems (tablets; contraceptive medicine based on progestational agent and estrogen)

IT 50-28-2D, Estradiol, ethers and esters

58652-20-3, Nomegestrol acetate

58691-88-6D, Nomegestrol, ethers and esters

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(contraceptive medicine based on progestational agent and estrogen)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Laboratoire Theramex; FR 2754179 A 1998 HCPLUS

L74 ANSWER 4 OF 15 HCPLUS COPYRIGHT 2002 ACS

AN 2000:854101 HCPLUS

DN 134:37255

TI Nomegestrol acetate and vascular reactivity: nonhuman primate experiments

AU Paris, J. M.; Williams, K. J.; Hermsmeyer, K. R.; Delansorne, R.

CS BP 59, Laboratoire Theramex, 98007, Monaco

SO Steroids (2000), 65(10-11), 621-627

CODEN: STEDAM; ISSN: 0039-128X

PB Elsevier Science Inc.

DT Journal

LA English

CC 2-4 (Mammalian Hormones)

AB Prevention of coronary artery disease has been recognized as a major

benefit of estrogen replacement therapy (ERT) in postmenopausal women. However, endometrial hyperplasia induced by unopposed ERT has raised important safety concerns. Progesterone or synthetic progestins have been used in combined hormone replacement therapy (HRT) to prevent endometrial cancer risk. Therefore, a major concern has been to ensure that the vascular beneficial effects of estrogens are not opposed when combined with progestins. **Nomegestrol acetate** (NOMAC) is an orally active progestin widely prescribed for HRT. Its vascular effects were evaluated in two models of coronary vascular reactivity in primates: the paradoxical vasoconstriction to acetylcholine (Ach) coronary infusion after 5 mo of mildly atherogenic diet in ovariectomized (OVX) Cynomolgus monkeys and the pharmacol. evoked coronary vasospasm in the OVX Rhesus monkey. In the first model, after 3 mo of continuous oral administration in the diet at 0.1 mg/kg/day, E2 prevented the paradoxical response to Ach, alone as well as combined with 0.25 mg/kg/day NOMAC, whereas NOMAC counteracted the endometrial stimulation. In the second model, after one artificial cycle consisting of 28 days of E2 s.c. implant and of daily oral gavage with 1 mg/kg/day of NOMAC for the last 14 days, no vasospasm (0 of 11 tested animals) occurred when the complete challenge protocol, including serotonin and the thromboxane agonist U46619, was administered to OVX Rhesus monkeys. In the balanced crossover design, identical artificial cycles with medroxyprogesterone acetate (MPA) at the same dose resulted in 7 vasospasms in 12 animals. In parallel, effective progestative activity was demonstrated by a secretory pattern in endometrial sections obtained at the end of the cycle. In these two nonhuman primate cardiovascular models, NOMAC did not have the negating effects obsd. with MPA.

ST  **nomegestrol acetate estradiol HRT**  
 postmenopause blood vessel endometrium monkey

IT Artery, disease  
 (coronary, spasm;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Artery, disease  
 (coronary;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Uterus, disease  
 (endometrium, hyperplasia;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Uterus  
 (endometrium;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Lipoproteins  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (high-d., cholesterol ester-contg.;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Blood plasma  
 Hormone replacement therapy  
 Vasoconstriction  
 ( **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Estrogen receptors  
 Glycerides, biological studies  
 Progesterone receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 ( **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT Menopause

(postmenopause;  **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT 50-28-2, **Estradiol**, biological studies 71-58-9,  
**Medroxyprogesterone acetate** 58652-20-3, **Nomegestrol acetate**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 ( **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

IT 57-88-5, **Cholesterol**, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 ( **nomegestrol acetate** and vascular reactivity in nonhuman primates in relation to role of progestins in hormone replacement therapy)

RE.CNT 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L74 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2000:790346 HCAPLUS

DN 133:330062

TI **Contraceptive compositions containing 2,1-benzisothiazoline 2,2-dioxides and progestational**

IN Grubb, Gary S.; Zhi, Lin; Jones, Todd K.; Marschke, Keith B.; Tegley, Christopher M.

PA American Home Products Corporation, USA; Ligand Pharmaceuticals, Inc.  
 SO PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K045-06

ICS A61K031-57; A61P015-18; A61K031-57; A61K031-425; A61K031-565  
 CC 2-3 (Mammalian Hormones)  
 Section cross-reference(s): 28, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000066163	A1	20001109	WO 2000-US11642	20000501
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US	6319912	B1	20011120	US 2000-552038	20000419
EP	1173209	A1	20020123	EP 2000-928610	20000501
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI US 1999-183023 P 19990504  
 US 2000-552038 A1 20000419  
 WO 2000-US11642 W 20000501

OS MARPAT 133:330062

AB This invention relates to cyclic **combination** therapies utilizing, in **combination** with a progestin, an **estrogen**, or both, and progesterone receptor antagonists 2,1-benzisothiazoline 2,2-dioxides. 5-(3-Chlorophenyl)spiro[2,1-benzisothiazole-3(1H),1'-cyclohexane] 2,2-dioxide was prep'd. and the antiprogestational activity of this compd. was demonstrated in a conventional pharmacol. test.

ST **contraceptive progestagen benzisothiazoline dioxide**

IT Progestogens

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antiprogestins; **contraceptive compns.** contg.  
 2,1-benzisothiazoline 2,2-dioxides and progestationals)

IT **Contraceptives**

(**contraceptive compns.** contg. 2,1-benzisothiazoline  
 2,2-dioxides and progestationals)

IT 304681-96-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (**contraceptive compns.** contg. 2,1-benzisothiazoline  
 2,2-dioxides and progestationals)

IT 628-77-3, 1,5-Diiodopentane 76513-69-4, 2-(Trimethylsilyl)ethoxymethyl chloride 111248-89-6

RL: RCT (Reactant)

(**contraceptive compns.** contg. 2,1-benzisothiazoline  
 2,2-dioxides and progestationals)

IT 304681-97-8P 304681-98-9P 304681-99-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (**contraceptive compns.** contg. 2,1-benzisothiazoline  
 2,2-dioxides and progestationals)

IT 51-98-9, Norethindrone acetate 68-22-4, Norethindrone 427-51-0, Cyproterone acetate 797-63-7, Levonorgestrel 6533-00-2, Norgestrel 35189-28-7, Norgestimate 53016-31-2, 17-Deacetyl norgestimate 54024-22-5, Desogestrel 54048-10-1, 3-Ketodesogestrel 58691-88-6, **Nomegestrol** 60282-87-3, Gestodene 65928-58-7, Dienogest 67392-87-4, Drospirenone 74513-62-5, Trimegestone 105149-04-0, Osaterone

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**contraceptive compns.** contg. 2,1-benzisothiazoline  
 2,2-dioxides and progestationals)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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L74 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:193986 HCAPLUS

DN 130:213664

TI Hormonal contraceptive

IN Hesch, Rolf-Dieter

PA Germany

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA German

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9912531	A2	19990318	WO 1998-DE2636	19980903
WO 9912531	A3	19990923		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19739916	A1	19990318	DE 1997-19739916	19970911
DE 19739916	C2	20010913		
AU 9911409	A1	19990329	AU 1999-11409	19980903
EP 1011682	A2	20000628	EP 1998-954135	19980903
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI DE 1997-19739916 A		19970911		
WO 1998-DE2636 W		19980903		
AB A hormonal contraceptive comprises a 1st hormonal component contg. .gtoreq.1 gestagen or antigestagen and a 2nd hormonal component contg. .gtoreq.1 estrogen or antiestrogen, for continuous and combined administration. This compn . inhibits ovulation and guarantees high contraceptive efficiency and reliable suppression of the menstrual cycle at very low doses, and can be used to treat mammary tumors. Continuous administration of estrogen favorably affects premenstrual syndrome and does not alter the equil. in the blood coagulation system, thereby avoiding the risk of thrombosis. The hormones may be administered orally, transdermally, intravaginally, or as sustained-release injections or implants. Thus, daily consumption of a tablet contg. 5 .mu.g ethynodiol diacetate and 2 mg norethisterone acetate by women for 9 mo provided good contraception and complete suppression of menstruation with practically no side effects.				

ST contraceptive female estrogen gestagen

IT Breast tumor inhibitors

**Contraceptives**

    Implants (drug delivery systems)

    Oral contraceptives

    Oral drug delivery systems

    Transdermal drug delivery systems

    Vaginal drug delivery systems

    (hormonal contraceptive)

IT Antiestrogens

Antiprogestins

**Estrogens****Progestins**

RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (hormonal contraceptive)

IT Sustained release drug delivery systems  
 (injections; hormonal contraceptive)

IT Injections (drug delivery systems)  
 (sustained release; hormonal contraceptive)

IT 50-27-1, Estriol 50-28-2, 17.beta.-Estradiol,  
 biological studies 51-98-9, Norethisterone acetate 52-76-6,  
 Lynestrenol 53-16-7, Estrone, biological studies 57-63-6,  
 Ethynodiol diacetate 57-83-0, Progesterone, biological studies 57-91-0,  
 17.alpha.-Estradiol 71-58-9, Medroxyprogesterone acetate  
 72-33-3, Mestranol 302-22-7, Chlormadinone acetate 427-51-0,  
 Cyproterone acetate 797-63-7, Levonorgestrel 979-32-8,  
 Estradiol valerate 5630-53-5, Tibolone 10540-29-1, Tamoxifen  
 24749-37-9, Estrane 54024-22-5, Desogestrel 58652-20-3,  
 Lutanyl 84371-65-3, RU 486 84449-90-1, Raloxifene  
 RL: BAC (Biological activity or effector, except adverse); BIOL  
 (Biological study)  
 (hormonal contraceptive)

L74 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:59650 HCAPLUS

DN 130:134273

TI **Contraceptive potential of a mifepristone-nomegestrol acetate sequential regimen in women**

AU Croxatto, Horacio B.; Salvatierra, Ana M.; Fuentealba, Blanca; Massai, Rebeca

CS Inst. Chileno de Medicina Reproductiva (ICMER), Santiago, Chile

SO Hum. Reprod. (1998), 13(12), 3297-3302

CODEN: HUREEE; ISSN: 0268-1161

PB Oxford University Press

DT Journal

LA English

CC 2-3 (Mammalian Hormones)

AB The effectiveness of a **sequential** regimen consisting of mifepristone, 10 mg/day for 15 days, followed by **nomegestrol acetate** (NOMA), 5 mg/day for the next 13 days, for inhibiting ovulation and maintaining regular bleeding cycles was assessed in 10 surgically sterilized volunteers who were followed for one pretreatment and three treated cycles. Hormonal detns. in blood and urine, ovarian ultrasonog., bleeding records in all cycles and an endometrial biopsy taken on day 22-25 of the third treatment cycle were used to monitor the effects of treatment. During treatment, 24 monophasic (no sustained progesterone rise above 12 nmol/l) and six biphasic cycles were recorded. Nine follicular ruptures were detected echog. in these 30 treated cycles, five of which occurred in monophasic cycles. All follicular ruptures occurred on days 1-7 of NOMA treatment. Echog. and endocrine features of ovulatory cycles were both present in only four treated cycles (13.3%). Development of a secretory endometrium was achieved in all cases, but it was always irregular. Regular withdrawal bleeding occurred in all subjects and no adverse reactions were recorded. The ovarian and endometrial effects of this regimen justify testing its **contraceptive** effectiveness in phase 2 clin. trials.

ST mifepristone nomegestrol acetate oral  
**contraceptive** ovulation inhibition ovary endometrium

IT Ovulation  
 (inhibition; mifepristone nomegestrol acetate  
 sequential regimen and its **contraceptive** potential in women)

IT Endometrium (uterus)  
 Menstruation  
**Oral contraceptives**  
 Ovarian cycle

Ovarian follicle  
 (mifepristone nomegestrol acetate  
 sequential regimen and its contraceptive potential in  
 women)

IT 58652-20-3, Lutetyl 84371-65-3, Ru486  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (mifepristone nomegestrol acetate  
 sequential regimen and its contraceptive potential in  
 women)

IT 50-28-2, Estradiol, biological studies 57-83-0,  
 Progesterone, biological studies 9002-67-9, LH  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (mifepristone nomegestrol acetate  
 sequential regimen and its contraceptive potential in  
 women)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (9) H; Hum Reprod 1993, V8, P201
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- (19) Neulen, J; Hum Reprod 1996, V11, P1533 HCAPLUS
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- (21) van Uem, J; Contraception 1989, V40, P171 HCAPLUS

L74 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:787662 HCAPLUS

DN 130:163331

TI Coadministration of nomegestrol acetate does not  
 diminish the beneficial effects of estradiol on coronary artery  
 dilator responses in nonhuman primates (Macaca fascicularis)

AU Williams, J. Koudy; Cline, J. Mark; Honore, Erika K.; Delansorne, Remi;  
 Paris, Jacques

CS Department of Comparative Medicine of Wake Forest, University School of  
 Medicine, Winston-Salem, NC, 27157-1040, USA

SO Am. J. Obstet. Gynecol. (1998), 179(5), 1288-1294  
 CODEN: AJOGAH; ISSN: 0002-9378

PB Mosby, Inc.

DT Journal

LA English

CC 2-4 (Mammalian Hormones)

AB Our purpose was to examine the effect of coadministered  
 nomegestrol acetate on estradiol-induced  
 dilator responses of coronary arteries. In this prospective randomized  
 trial, ovariectomized monkeys were fed a moderately atherogenic diet for 3  
 mo while being treated with (1) no hormone replacement (control), (2)  
 estradiol (1.5 mg/d equiv.) added to the diet, or (3)  
 estradiol (1.5 mg/d equiv.) plus nomegestrol  
 acetate (3.75 mg/d equiv.) added to the diet. Effects of  
 treatment were measured with anal. of variance. Post hoc analyses were

done by multiple comparison tests with Bonferroni corrections. Constrictor responses of epicardial coronary arteries (measured with quant. angiog.) and decreased coronary blood velocity (measured with Doppler ultrasonog.) to acetylcholine (10-6 mol/L) were less in the estradiol-treated monkeys (with or without cotreatment with nomegestrol acetate) than in the untreated monkeys.

Typical estrogenic responses were induced by estradiol in the endometrium (i.e., increased proliferation (Ki-67 expression) and increased hormone receptor expression). These effects were antagonized by nomegestrol acetate. Although nomegestrol acetate has typical progestin-like effects on the uterus, it does not diminish the beneficial effects of estrogen on acetylcholine-induced dilator responses of coronary arteries.

ST nomegestrol acetate estradiol coronary artery vasodilation

IT Coronary blood flow (estradiol and nomegestrol acetate effect on coronary circulation response to acetylcholine in nonhuman primates)

IT Coronary artery (nomegestrol acetate coadministration does not diminish estradiol beneficial effects on coronary artery dilator responses in nonhuman primates)

IT 51-84-3, Acetylcholine, biological studies  
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(estradiol and nomegestrol acetate effect on coronary circulation response to acetylcholine in nonhuman primates)

IT 50-28-2, Estradiol, biological studies

58652-20-3, Nomegestrol acetate

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(nomegestrol acetate coadministration does not diminish estradiol beneficial effects on coronary artery dilator responses in nonhuman primates)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Adams, M; Arterioscler Thromb Vasc Biol 1997, V17, P217 HCAPLUS
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- (3) Barrett-Connor, E; JAMA 1991, V265, P1861 MEDLINE
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- (25) Williams, J; J Am Coll Cardiol 1994, V24, P1757 HCAPLUS
- (26) Wilson, M; Endocrinology 1988, V123, P2653 HCAPLUS

DN 129:49807  
 TI Insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with **estradiol** alone or **combined** with **nomegestrol acetate**  
 AU Wagner, Janice D.; Thomas, Michael J.; Williams, J. Koudy;  
 Zhang, Li; Greaves, Kathryn A.; Cefalu, William T.  
 CS Department of Comparative Medicine, Bowman Gray School of Medicine,  
 Winston-Salem, NC, 27157-1040, USA  
 SO J. Clin. Endocrinol. Metab. (1998), 83(3), 896-901  
 CODEN: JCEMAZ; ISSN: 0021-972X  
 PB Endocrine Society  
 DT Journal  
 LA English  
 CC 2-4 (Mammalian Hormones)  
 AB The authors have previously shown that medroxyprogesterone acetate (MPA), either alone or **combined** with conjugated equine **estrogens** (CEE), significantly decreased insulin sensitivity (SI), compared with both untreated controls and those treated with CEE alone. The purpose of this study was to det. the effects of **estradiol** (E2), with and without **nomegestrol acetate** (NA; a potent progestin that lacks androgenic activity), on SI and arterial antioxidant activity, as detd. by F2-isoprostanes. Thirty-six adult female cynomolgus monkeys (*Macaca fascicularis*) were ovariectomized and fed a moderately atherogenic diet, with one of the following three treatments added to the diet, for 12 wk: (1) no treatment (control); (2) E2; or (3) continuous **combined** E2 + NA. SI and glucose effectiveness were assessed by the frequently sampled i.v. glucose tolerance test using a third-phase insulin infusion after 10 wk of treatment. Cholesterol content and F2-isoprostanes were measured in the thoracic aorta after 12 wk of treatment. E2 treatment resulted in a significantly greater SI, compared with control or E2+NA-treated monkeys (10.03 vs. 35 and 6.49 .times. 10<sup>-4</sup> min<sup>-1</sup> .mu.U-1mL). In contrast to the authors' studies of CEE and MPA, E2+NA treatment, though reducing the SI below that of the E2 group, did not reduce the SI below that of control monkeys. As expected, the short period of treatment resulted in no significant differences in aortic cholesterol content. There was no treatment effect on total F2-isoprostanes (representing F2-isoprostane formation caused primarily by autoxidn.), suggesting minimal antioxidant activity. However, there was a treatment difference in the prostaglandin F2.alpha. (PGF2.alpha.) isomer (a prostaglandin (PG) isomer formed by both autoxidn. of arachidonate and cyclooxygenase activity). PGF2.alpha. concns. were 32% lower with E2 treatment, compared with controls, and 36% lower, compared with E2+NA treatment (0.48 vs. 71 and 0.75), suggesting differences in PG synthesis between hormone treatments. In conclusion, NA, a progestin without androgenic activity, may still affect some cardiovascular risk factors differently than **estrogen**-only therapy. However, it seems to be less detrimental than MPA.  
 ST insulin cardiovascular risk **estradiol nomegestrol**  
 monkey  
 IT Prostaglandins  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (F2-isoprostanes; insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with **estradiol** alone or **combined** with **nomegestrol acetate**)  
 IT Antioxidants  
 Artery  
 Atherosclerosis  
 Cardiovascular agents  
*Macaca fascicularis*  
 Thoracic aorta  
 (insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with **estradiol** alone or **combined** with **nomegestrol acetate**)  
 IT Blood cholesterol  
 Low-density lipoproteins  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with estradiol alone or combined with nomegestrol acetate)

IT 9004-10-8, Insulin, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with estradiol alone or combined with nomegestrol acetate)

IT 50-28-2, Estradiol, biological studies  
 58691-88-6, Nomegestrol  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with estradiol alone or combined with nomegestrol acetate)

IT 551-11-1, PGF2.alpha.  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with estradiol alone or combined with nomegestrol acetate)

IT 50-99-7, Glucose, biological studies  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (tolerance; insulin sensitivity and cardiovascular risk factors in ovariectomized monkeys with estradiol alone or combined with nomegestrol acetate)

L74 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2002 ACS

AN 1998:239116 HCAPLUS

DN 128:312905

TI Pharmaceutical composition consisting of an estrogen and a progestogen

IN Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis

PA Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis

SO PCT Int. Appl., 22 pp.

CODEN: PIXXD2

DT Patent

LA French

IC ICM A61K031-57

ICS A61K031-57; A61K031-565

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 2

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9815279	A1	19980416	WO 1997-FR1792	19971008 <--
	W: AU, BR, CA, CN, CU, CZ, HU, ID, IL, JP, KR, MG, MX, NO, NZ, PL, RO, RU, SG, SK, TR, US, VN, YU				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2754179	A1	19980410	FR 1996-12239	19961008 <--
	FR 2754179	B1	19981224		
	AU 9746273	A1	19980505	AU 1997-46273	19971008 <--
	ZA 9709011	A	19980603	ZA 1997-9011	19971008 <--
	BR 9712274	A	19990831	BR 1997-12274	19971008 <--
	EP 956022	A1	19991117	EP 1997-944940	19971008 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1239893	A	19991229	CN 1997-180380	19971008 <--
	NO 9901593	A	19990607	NO 1999-1593	19990331 <--
	KR 2000048981	A	20000725	KR 1999-703032	19990408 <--
PRAI	FR 1996-12239	A	19961008 <--		
	WO 1997-FR1792	W	19971008 <--		
AB	The invention concerns the field of chem. therapy and more particularly				

the field of pharmaceutical hormonal technique. More precisely it concerns novel pharmaceutical hormonal compns. characterized in that they are formed by an **estrogen**-progestogen combination assocd. or mixed with 1 or several nontoxic, inert and excipients, for oral administration. The combined assocn. can be prescribed continuously or intermittently, for producing a compn. for treating **estrogenic** deficiencies, preventing osteoporosis and cardiovascular diseases in menopausal women, or still for blocking **ovulation** in a woman during the period of **ovarian** activity. Thus, tablets contained **estradiol** 1.5, **namegestrol acetate** 2.5, Avicel PH-102 22.4, lactose 60, PVP 8.4, colloidal silica 1.2, glycerol palmitostearate 3.6, and dye 0.4 mg. The effectiveness of this combination in the treatment of diseases in menopausal women was demonstrated.

ST **estrogen** progestogen pharmaceutical

IT Cardiovascular diseases

Menopause

Osteoporosis

**Ovulation**

(pharmaceutical compn. consisting of an **estrogen** compd. and of a progestogen)

IT Progestins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compn. consisting of an **estrogen** compd. and of a progestogen)

IT **Estrogens**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compn. contg. **estrogen** and progestogen)

IT 50-28-2, **Estradiol**, biological studies 50-28-2D

, **Estradiol**, derivs. 979-32-8, **Estradiol** valerate

58652-20-3, **Namegestrol acetate**

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compn. consisting of an **estrogen** compd. and of a progestogen)

L74 ANSWER 11 OF 15 HCPLUS COPYRIGHT 2002 ACS

AN 1997:229672 HCPLUS

DN 126:272509

TI Impact of percutaneous **estradiol** gels in postmenopausal hormone replacement therapy on clinical symptoms and endometrium

AU Foidart, Jean-Michel; Beliard, Aude; Hedon, Bernard; Ochsenbein, Edith; Bernard, Anne-Marie; Bergeron, Christine; Thomas, Jean-Louis

CS Laboratory of Biology, Centre Hospitalier du Bois de l'Abbaye, University of Liege and Department of Obstetrics and Gynaecology, Seraing, Belg.

SO Br. J. Obstet. Gynaecol. (1997), 104(3), 305-310

CODEN: BJOGAS; ISSN: 0306-5456

PB Blackwell

DT Journal

LA English

CC 2-4 (Mammalian Hormones)

AB Our objective was to compare the effects on endometrium, climacteric symptoms and the menstrual cycle, and the clin. and biol. tolerance of two percutaneous **estradiol** gels used as hormone replacement therapy. Two-hundred and fifty-four women with an intact uterus and who had experienced a natural menopause received either Oestrogel (n = 126) or Estreva a new formulation of **estradiol** gel (n = 128), (1.5 mg of **estradiol**/day) for the 24 first days of each calendar month during six consecutive months. **Namegestrol acetate** (

**Lutetyl**), a norprogesterone deriv., was administered (5 mg/day) from day 11 to day 24 of each **estradiol** cycle. Examm. of endometrial biopsies taken before treatment and between days 18 and 24 of the last treatment cycle, climacteric symptoms assessed using a modified Kupperman index, control of menstrual cycle evaluated by diary cards, and clin. and biol. tolerance. Both treatments lowered the frequency and intensity of hot flushes and the global Kupperman index. 96% of the

cycles were followed by withdrawal bleeding. Breakthrough bleeding or spotting resulted in premature discontinuation of treatment in one volunteer. Mastodynia occurred in 20 women and contributed to the premature termination of treatment in three of them. Endometrial biopsies taken at the end of treatment showed identical histologies in both groups, with a secretory pattern in the majority of women, and absence of hyperplasia. This trial confirmed that, when the two estradiol gels tested were administered cyclically with nomegestrol acetate to postmenopausal women, they were well tolerated, effective and suitable for the treatment of estrogen deficiency syndrome.

ST estradiol endometrium postmenopause hormone replacement therapy  
 IT Endometrium (uterus)  
 Postmenopause  
 (impact of percutaneous estradiol gels in postmenopausal hormone replacement therapy on clin. symptoms and endometrium in humans)  
 IT Hormones (animal), biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (replacement therapy; impact of percutaneous estradiol gels in postmenopausal hormone replacement therapy on clin. symptoms and endometrium in humans)  
 IT 50-28-2, Estradiol, biological studies  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (impact of percutaneous estradiol gels in postmenopausal hormone replacement therapy on clin. symptoms and endometrium in humans)

L74 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1997:226799 HCAPLUS  
 DN 126:216684  
 TI Novel hormonal medicaments and use thereof for correcting estrogen deficiencies  
 IN Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis  
 PA Laboratoire Theramex, Monaco; Lanquetin, Michel; Paris, Jacques; Thomas, Jean-Louis  
 SO PCT Int. Appl., 19 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA French  
 IC ICM A61K031-57  
 ICI A61K031-57, A61K031-565  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9704784	A1	19970213	WO 1996-IB754	19960729	<--
	W: AU, BR, CA, CN, CZ, FI, HU, IL, JP, KR, MX, NO, RU, SG, US, VN					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	FR 2737411	A1	19970207	FR 1995-9364	19950801	<--
	FR 2737411	B1	19971017			
	CA 2201368	AA	19970213	CA 1996-2201368	19960729	<--
	AU 9663674	A1	19970226	AU 1996-63674	19960729	<--
	AU 722355	B2	20000727			
	EP 783310	A1	19970716	EP 1996-923018	19960729	<--
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	CN 1167438	A	19971210	CN 1996-191100	19960729	<--
	BR 9606549	A	19980623	BR 1996-6549	19960729	<--
	JP 10507207	T2	19980714	JP 1996-507406	19960729	<--
	ZA 9606545	A	19970508	ZA 1996-6545	19960801	<--
	NO 9701449	A	19970530	NO 1997-1449	19970326	<--

PRAI US 5891867 A 19990406 US 1997-817329 19970424 <--  
 FR 1995-9364 A 19950801 <--  
 WO 1996-IB754 W 19960729 <--  
 AB A trisquential, oestroprogesterone hormonal combination characterized in that it comprises unit doses contg. only one **estrogen**, unit doses contg. a combination of one **estrogen** and one progestogen, and unit doses contg. only one carrier. The trisquential delivery mode aims at compensating functional disorders caused by menopausal or pre-menopausal **hypoestrogenism**. Formulation of 1.5 mg 17.β-**estradiol** tablets and 2.5 mg **namegestrol acetate** tablets are disclosed. The efficacy of tablets in treatment of hot flashes in menopausal women are reported.  
 ST pharmaceutical tablet **estrogen** deficiency progestogen  
 IT Glycerides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (C16-18; novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT **Estrogen** deficiency  
 Menopause  
 Tablets (drug delivery systems)  
 (novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT **Estrogens**  
 Progestins  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT 9004-34-6, Cellulose, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (microcryst.; novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT 50-28-2, 17.β-**Estradiol**, biological studies  
 35380-71-3, **Estradiol** hemihydrate 58652-20-3,  
**Namegestrol acetate**  
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT 67-63-0, Isopropyl alcohol, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (novel hormonal medicaments for correcting **estrogen** deficiencies)  
 IT 63-42-3, Lactose 7631-86-9, Silica, biological studies 9003-39-8, Pvp  
 9003-39-8D, Pvp, crosslinked  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (novel hormonal medicaments for correcting **estrogen** deficiencies)  
 L74 ANSWER 13 OF 15 HCPLUS COPYRIGHT 2002 ACS  
 AN 1996:746706 HCPLUS  
 DN 126:42825  
 TI The antigenadotrophic activity of progestins (19-nortestosterone and 19-norprogesterone derivatives) is not mediated through the androgen receptor  
 AU Couzinet, Beatrice; Young, Jacques; Brailly, Sylvie; Chanson, Philippe; Thomas, Jean Louis; Schaison, Gilbert  
 CS Service Endocrinologie Maladies Reproduction, Hop. Bicetre, Kremlin, 94275, Fr.  
 SO J. Clin. Endocrinol. Metab. (1996), 81(12), 4218-4223  
 CODEN: JCCEMAZ; ISSN: 0021-972X  
 PB Endocrine Society  
 DT Journal  
 LA English  
 CC 2-4 (Mammalian Hormones)  
 AB To further study the mechanism of the antigenadotrophic activity of

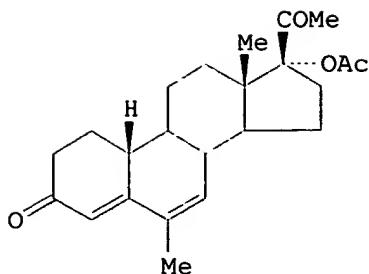
progestins, the effects of a 19-nortestosterone deriv., norethisterone acetate (NETA), and a 19-norprogesterone deriv., **nomegestrol acetate** (NOMA), were compared. The aim was to assess whether their action is exerted via the androgen receptor. Ten healthy postmenopausal women were treated for five monthly periods of 24 days sep'd. by 10 days in a randomized crossover design. Transdermal **estradiol**, Estraderm TTS (25 .mu.g; one patch every 3 days), was given from days 1-24 during the five periods. On the last 12 days, of each **estradiol** treatment, they all received a placebo, NOMA (5 mg/day), NOMA in assocn. with the nonsteroidal antiandrogen, flutamide (FLU; 250 mg, twice a day), NETA (10 mg/day), or NETA plus FLU. On the other hand, three castrated patients with complete androgen insensitivity (CAI) received NOMA and NETA for two periods of 12 days sep'd. by 3 wk. In postmenopausal women, the effects of NOMA and NETA on metabolic parameters were studied. Only NETA decreased high d. lipoprotein cholesterol. Plasma LH, FSH, and **estradiol** were measured during each treatment period. A significant decrease in mean plasma LH and FSH levels and their responses to exogenous GnRH was obsd. with NOMA and NETA treatments compared to placebo. The pulsatile frequency, but not the amplitude, of LH was significantly decreased during both treatments. Interestingly, the effects of both progestins on gonadotropins were not antagonized by FLU administration. In the patients with CAI, the pulsatile study of gonadotropins was performed before and on day 12 of NOMA and NETA treatments. As in postmenopausal women, both progestins induced similar decreases in LH and FSH. In conclusion, a 19-nortestosterone deriv., NETA, and a 19-norprogesterone deriv., NOMA, have similar antigenadotropic activities. This effect, not antagonized by FLU and obsd. in patients with CAI, is not mediated via the androgen receptor. The absence of deleterious effects of 19-norprogesterone derivs. on metabolic parameters should favor the therapeutic use of these compds.

ST antigenadotropic nortestosterone norprogesterone androgen receptor  
 IT Postmenopause  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT Progestins  
     RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT Androgen receptors  
     High-density lipoproteins  
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT Androgen insensitivity  
     RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT 9034-40-6, LH-RH 13311-84-7, Flutamide  
     RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT 50-28-2, **Estradiol**, biological studies  
     RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT 51-98-9, Norethisterone acetate 58652-20-3, **Nomegestrol acetate**  
     RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (antagonadotropic activity of progestins is not mediated by androgen receptor)  
 IT 57-88-5, Cholesterol, biological studies 9002-67-9, LH 9002-68-0, FSH

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (antigonadotropic activity of progestins is not mediated by androgen receptor)

L74 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1995:725440 HCAPLUS  
 TI Subdermal contraceptive implants  
 AU Peralta, Octavio; Diaz, Soledad; Croxatto, Horacio  
 CS Instituto Chileno de Medicina Reproductiva, Santiago, Chile  
 SO J. Steroid Biochem. Mol. Biol. (1995), 53(1-6), 223-6  
 CODEN: JSBBEZ; ISSN: 0960-0760  
 DT Journal  
 LA English  
 AB Subdermal contraceptive implants involve the delivery of a steroid progestin from polymer capsules or rods placed under the skin. The hormone diffuses out slowly at a stable rate, providing contraceptive effectiveness for 1-5 yr. The period of protection depends upon the specific progestin and the type of polymer. Advantages of progestin implants include long term contraceptive action without requiring the user's or provider's attention, low dose of highly effective contraception without the use of estrogen, and fertility is readily reversible after the removal of implants. The levonorgestrel implant Norplant R system is the only one that has been approved for distribution. The contraceptive efficacy of Norplant is the highest obsd. amongst the most effective methods with an annual pregnancy rate of 0.2 during the first and second year and 1.1 on the fifth year. Menstrual problems are the main reason for the discontinuation of Norplant and 9% of women stopped using it during the first year of treatment. Other implants are still under development trying to simplify the method by reducing the no. of units and to introduce other progestins that may minimize side effects. Norplant-2 was designed to release the same dose of progestin from only two covered rods. Evaluation of 1400 women enrolled, indicates that over 2 yr the cumulative pregnancy rate is below 0.5 per 100 women. There are three single implants under development: Nestorone, 3-Keto-desogestrel and Uniplant that are expected to be effective for 1-2 yr. Phase II clin. trials with Nestorone have been completed and no pregnancies have been obsd. in 1570 woman-months of use. Bleeding irregularities occurred in 20-30% of the women but there were only four terminations because of bleeding problems. A multicentric study is ongoing with a newly designed 3-keto-desogestrel implant named Implanon, which releases approx. 60 Mg/day of the hormone. The objectives of this study are to assess contraceptive efficacy, safety and acceptability of Implanon. Another multicentric study is ongoing with Uniplant, which releases nomegestrol acetate with a duration of action for only 1 yr. The objectives of the trial are to study the endocrine profile of Uniplant users and to evaluate the efficacy and acceptability of the method.

L74 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1987:149754 HCAPLUS  
 DN 106:149754  
 TI Effects of progesterone and nomegestrol acetate on rabbit endometrial epithelium. Scanning-electron-microscopic study  
 AU Paris, J. M.; Mrena, E.; Lanquetin, A.; Marchal, G. M.; Thevenot, R.  
 CS Lab. Theramex, Monaco, 98000, Monaco  
 SO J. Pharmacol. (1986), 17(4), 508-14  
 CODEN: JNPHAG; ISSN: 0021-793X  
 DT Journal  
 LA French  
 CC 2-4 (Mammalian Hormones)  
 GI



AB Priming of immature rabbits with **estradiol** [50-28-2] followed by injection of progesterone [57-83-0] (2-12.5 mg) s.c. for 5 days resulted in changes in endometrial morphol. as detected by SEM which were similar to the changes occurring in postmenopausal women on estroprogestative therapy. Similar changes were obsd. when **nomegestrol acetate** (I) [58652-20-3] (0.25-12.5 mg, orally) was substituted for progesterone. Thus, the 19-norprogesterone deriv. displayed similar activity to the parent compd.

ST uterus morphol progesterone **nomegestrol**; endometrium morphol progesterone **nomegestrol**

IT Uterus  
 (endometrium, epithelium, morphol. of, **estradiol** and **nomegestrol** and progesterone effect on)

IT Menopause  
 (post-, **estradiol** and **nomegestrol** and progesterone effect on endometrium morphol. in relation to)

IT 57-83-0, Progesterone, biological studies  
 RL: BIOL (Biological study)  
 (uterus endometrium morphol. response to **estradiol** and, **nomegestrol** in comparison with)

IT 58652-20-3, **Nomegestrol acetate**  
 RL: BIOL (Biological study)  
 (uterus endometrium morphol. response to **estradiol** and, progesterone in comparison with)

IT 50-28-2, **Estradiol**, biological studies  
 RL: BIOL (Biological study)  
 (uterus endometrium morphol. response to **nomegestrol** and progesterone and)

=> fil reg  
 FILE 'REGISTRY' ENTERED AT 11:55:27 ON 15 MAR 2002  
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STRUCTURE FILE UPDATES: 13 MAR 2002 HIGHEST RN 400796-85-2  
 DICTIONARY FILE UPDATES: 13 MAR 2002 HIGHEST RN 400796-85-2

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

The P indicator for Preparations was not generated for all of the

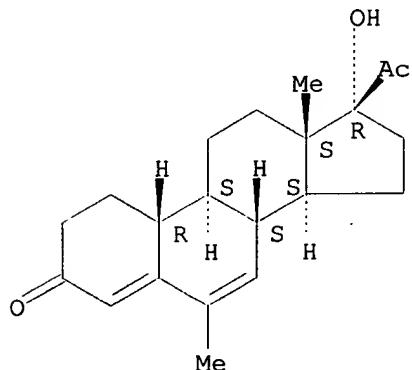
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to [help@cas.org](mailto:help@cas.org) for further assistance or to receive a credit for any duplicate searches.

=> d ide can 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
 RN 58691-88-6 REGISTRY  
 CN 19-Norpregna-4,6-diene-3,20-dione, 17-hydroxy-6-methyl- (9CI) (CA INDEX  
 NAME)  
 OTHER NAMES:  
 CN Nomegestrol  
 CN TX 071  
 FS STEREOSEARCH  
 MF C21 H28 O3  
 LC STN Files: ADISINSIGHT, ADISNEWS, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA,  
 CANCERLIT, CAPLUS, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE,  
 IPA, MEDLINE, PROMT, SYNTHLINE, TOXCENTER, USAN, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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 4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 23 REFERENCES IN FILE CAPLUS (1967 TO DATE)

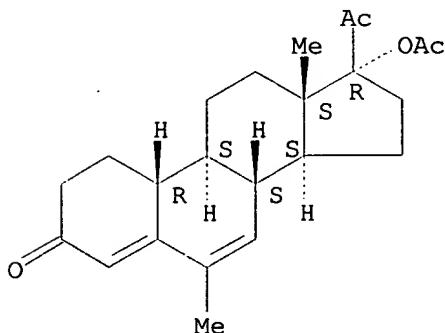
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REFERENCE 7: 133:330061  
 REFERENCE 8: 133:276797  
 REFERENCE 9: 132:44984  
 REFERENCE 10: 131:262597

=> d ide can 12

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
 RN 58652-20-3 REGISTRY  
 CN 19-Norpregna-4,6-diene-3,20-dione, 17-(acetoxy)-6-methyl- (9CI) (CA  
 INDEX NAME)  
 OTHER NAMES:  
 CN 6-Methyl-17.alpha.-acetoxy-.DELTA.6-19-norprogesterone  
 CN Lutetyl  
 CN Nomegestrol acetate  
 CN Surplant  
 CN TX 066  
 CN Uniplant  
 FS STEREOSEARCH  
 MF C23 H30 O4  
 LC STN Files: ADISINSIGHT, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
 BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMLIST, CIN, DDFU, DRUGPAT, DRUGU,  
 DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, PHAR,  
 PHARMASEARCH, PROMT, RTECS\*, SYNTHLINE, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: EINECS\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

65 REFERENCES IN FILE CA (1967 TO DATE)  
 66 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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 REFERENCE 2: 136:799  
 REFERENCE 3: 135:327515  
 REFERENCE 4: 135:298911  
 REFERENCE 5: 134:316160

REFERENCE 6: 134:316159  
REFERENCE 7: 134:173207  
REFERENCE 8: 134:51472  
REFERENCE 9: 134:37255  
REFERENCE 10: 134:36648

=> d ide can 15

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 50-28-2 REGISTRY  
CN Estra-1,3,5(10)-triene-3,17-diol (17. $\beta$ .)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Estradiol (8CI)  
OTHER NAMES:  
CN (+)-3,17. $\beta$ .-Estradiol  
CN . $\beta$ .-Estradiol  
CN 13. $\beta$ .-Methyl-1,3,5(10)-gonatriene-3,17. $\beta$ .-ol  
CN 17. $\beta$ .-Estradiol  
CN 17. $\beta$ .-Oestradiol  
CN 3,17-Epidihydroxyestratriene  
CN 3,17. $\beta$ .-Dihydroxyestra-1,3,5(10)-triene  
CN 3,17. $\beta$ .-Estradiol  
CN Aeradiol  
CN Altrad  
CN Aquadiol  
CN Bardiol  
CN Beta-estradiol  
CN Climaderm  
CN Climara  
CN Compudose  
CN Compudose 200  
CN Compudose 365  
CN Corpagen  
CN Dermestril  
CN Dihydrofollicular hormone  
CN Dihydrofolliculin  
CN Dihydromenformon  
CN Dihydrotheelin  
CN Dihydroxyestrin  
CN Dimenformon  
CN Diogyn  
CN Diogynets  
CN Divigel  
CN E 2  
CN Encore  
CN Epiestradiol 50  
CN Estra-1,3,5(10)-triene-3,17-diol, (17. $\beta$ .)-  
CN Estra-1,3,5(10)-triene-3,17. $\beta$ .-diol  
CN Estrace  
CN Estraderm  
CN Estraderm TTS  
CN Estraderm TTS 50  
CN Estraldine  
CN Estroclim 50  
CN Estrogel  
CN Estrovite  
CN Evorel  
CN Femestral

CN Femogen  
 CN Follicyclin  
 CN Ginosedol  
 CN Gynergon  
 CN Gynoestryl

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
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FS STEREOSEARCH  
 MF C18 H24 O2

CI COM

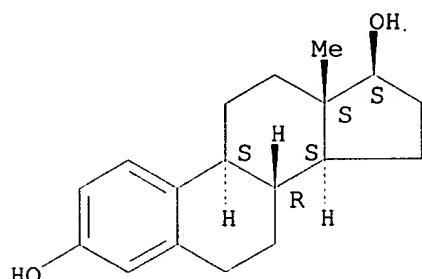
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 CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,  
 CSNB, DDFU, DETHERM\*, DIOGENES, DRUGNL, DRUGU, DRUGUPDATES, EMBASE,  
 GMELIN\*, HODOC\*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS,  
 NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS\*, SPECINFO,  
 SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

43197 REFERENCES IN FILE CA (1967 TO DATE)

780 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

43256 REFERENCES IN FILE CAPLUS (1967 TO DATE)

12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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